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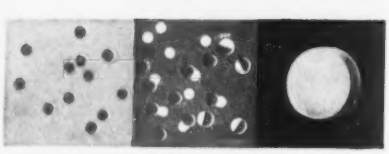

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* Wilkins, R. W.; Judson, W. E.; Stone, R. W.; Hollander, William; Huckabee, W. E., and Friedman, I. H.: Reserpine in the Treatment of Hypertension: A Note on the Relative Dosage and Effects, New England J. Med. 250:477 (March 18) 1954.

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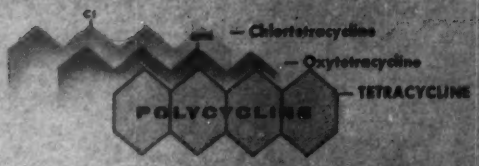

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1. Getz, H. R.; Westfall, I. S., and Henderson, H. J.: Nutrition in Tuberculosis as Evaluated by Blood Analysis, Am. Rev. Tuberc. *50*:96 (Aug.) 1944.
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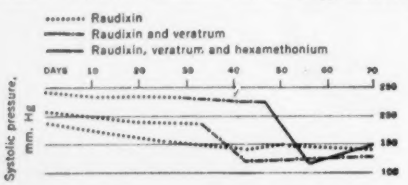

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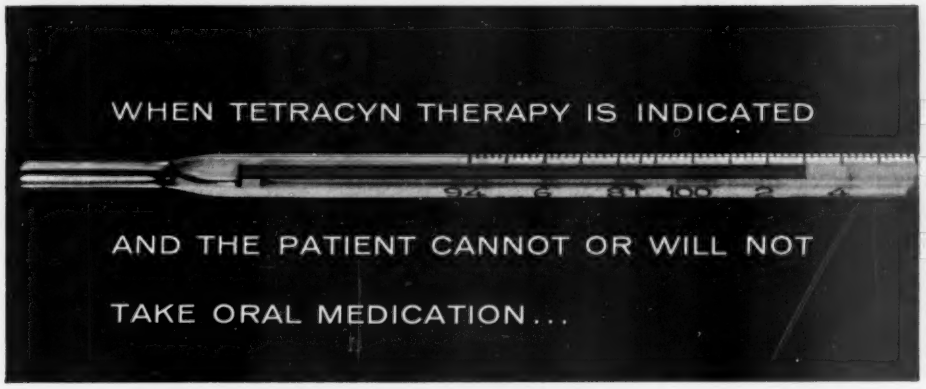

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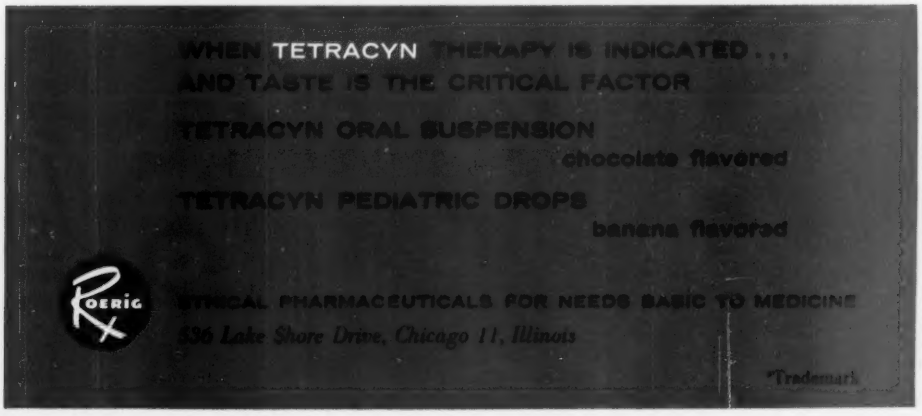

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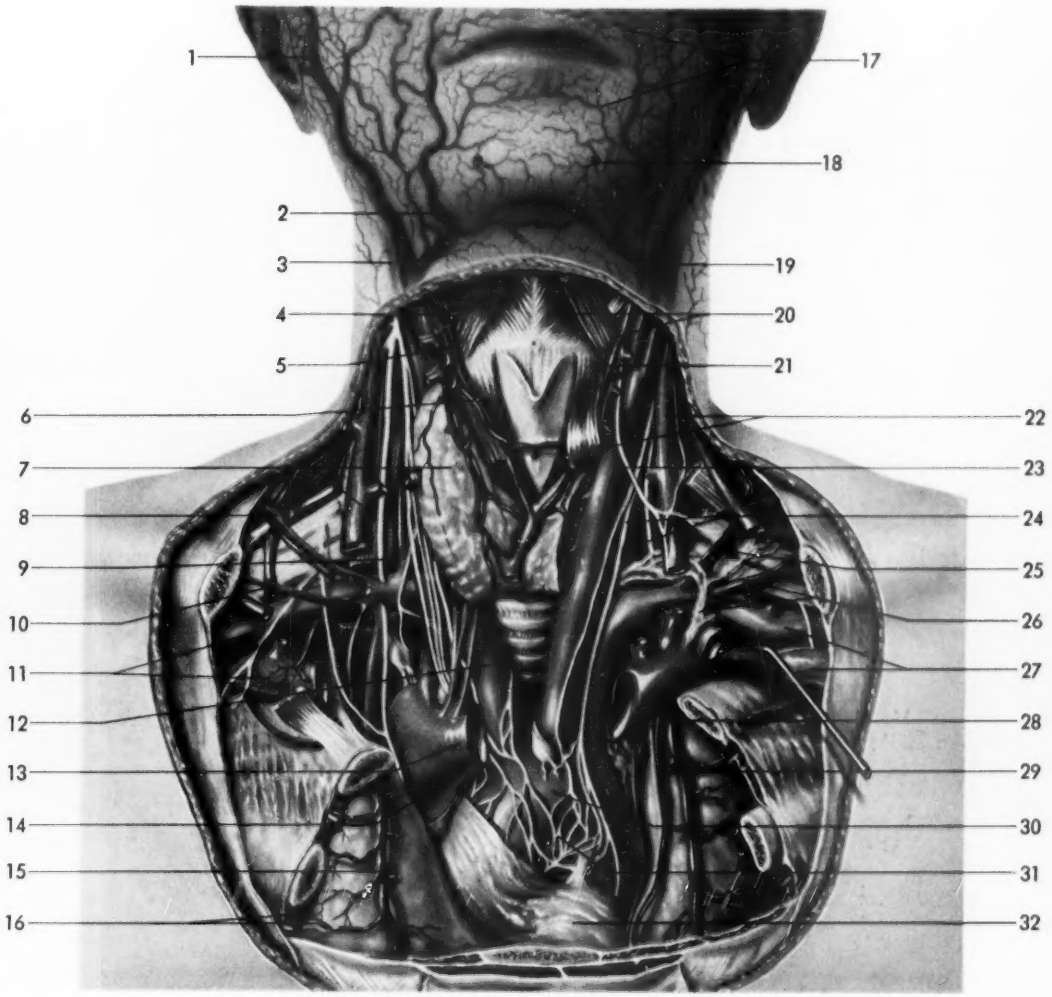

1 Superficial temporal artery
2 External maxillary artery
3 Internal carotid artery
4 Superior laryngeal artery
5 Right superior thyroid artery and vein
6 Cricothyroid branches of superior thyroid artery and vein
7 Internal jugular vein; thyroid gland
8 Right superficial cervical artery
9 Right inferior thyroid artery
10 Right suprascapular artery
11 Right subclavian artery and vein
12 Innominate artery
13 Left innominate vein
14 Superior vena cava
15 Right internal mammary artery
16 Anterior intercostal artery and vein
17 Superior and inferior labial arteries
18 Mental artery and mental foramen
19 External carotid artery
20 Mylohyoid muscle; left superior thyroid artery
21 Thyrohyoid muscle
22 Sternothyroid muscle; internal jugular vein
23 Left common carotid artery
24 Left inferior thyroid artery; vagus nerve
25 Left superficial cervical artery and vein
26 Left suprascapular artery; thoracic duct
27 Left subclavian artery and vein
28 Left internal mammary artery
29 Pericardiacophrenic artery
30 Aortic arch
31 Superficial cardiac plexus
32 Pericardium

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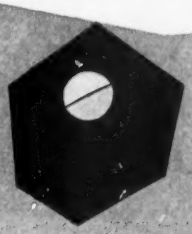

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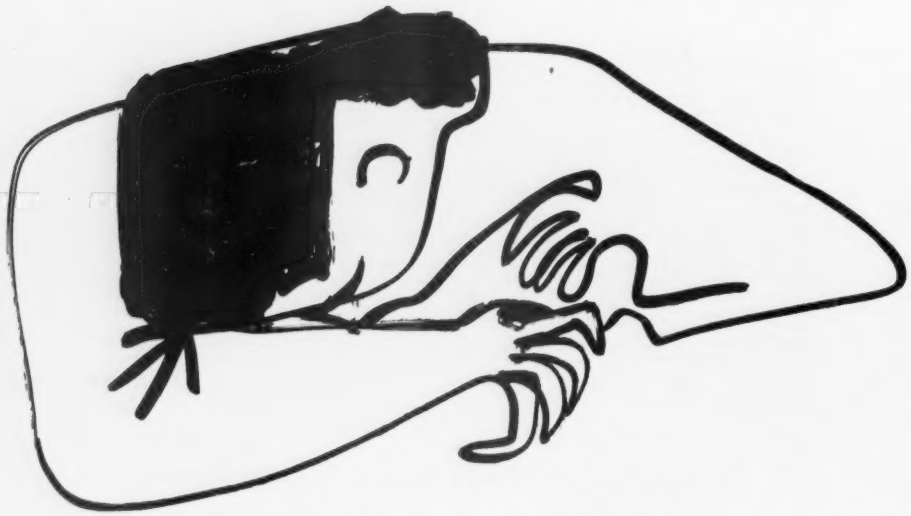

IN 50% of menstruating women,[1] emotional symptoms have a *physical* basis that you can treat *medically*. The syndrome of premenstrual tension — depression, irritability, anxiety, headaches, fatigue, mastalgia, edema — "cannot be dismissed as being neurotic or primarily psychogenic."[2]

Morton reports: *Effective in* 80-90% *of cases*,[3,4] "The greatest improvement was noted in the nervous and mental symptoms."[3]

1. Freed, S. C.: Internat. Rec. Med. 166:465 (Nov.) 1953. 2. Rees, L.: J. Ment. Sc. 99:62 (Jan.) 1953. 3. Morton, J. H., et al.: Am. J. Obst. & Gynec. 65:1182 (June) 1953. 4. Morton, J. H.: Internat. Rec. Med. 166:505 (Nov.) 1953.

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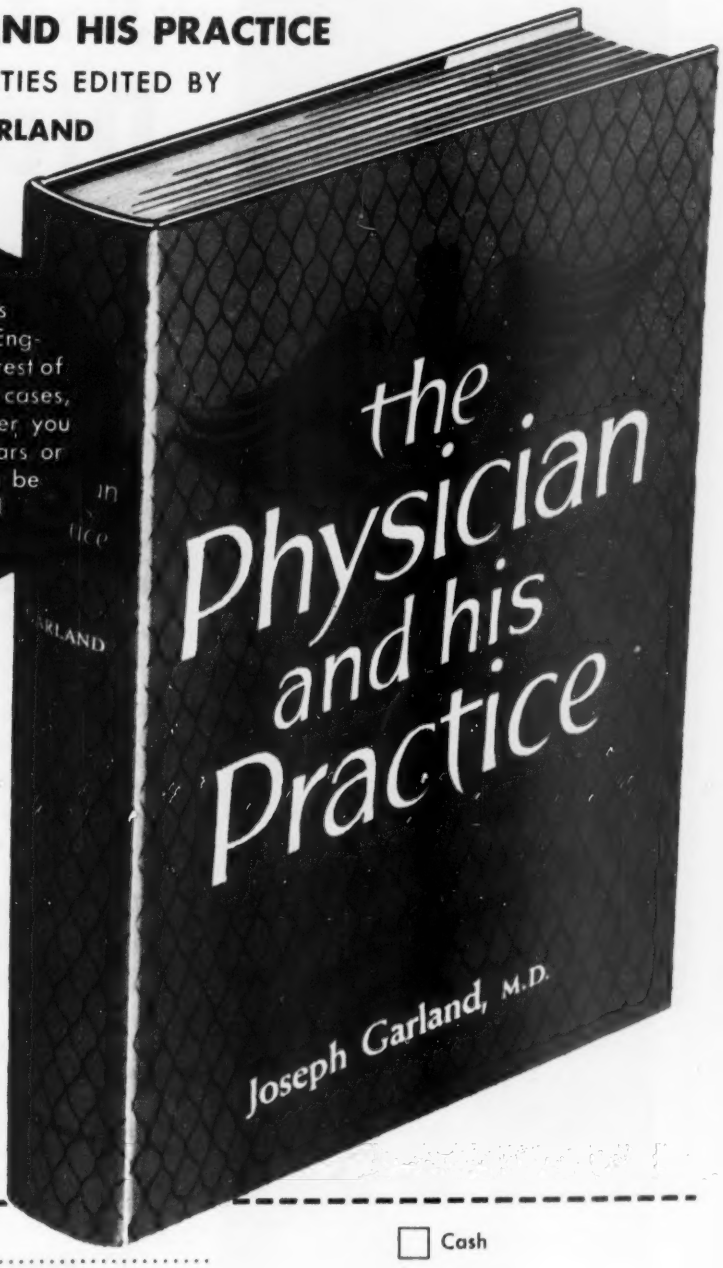

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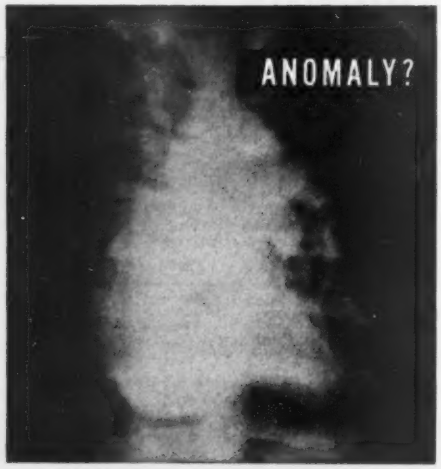

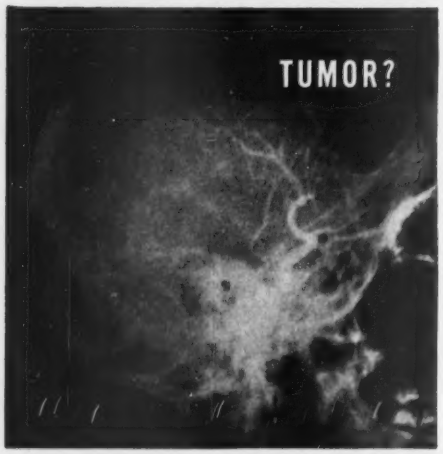

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Volume 251 SEPTEMBER 9, 1954 Number 11

POSTOPERATIVE WOUND INFECTIONS DUE TO *STAPHYLOCOCCUS AUREUS**

CHESTER W. HOWE, M.D.†

BOSTON

IT is probable that all surgical wounds are inoculated with bacteria at operation.[1-3] Whether or not sepsis develops depends on the summation of forces exerted by many factors. Among these are the invasive capacity of the organism, the resistance of the host, the size of the inoculum, the degree of excellence in surgical or antiseptic technic, the presence of physiologic derangements, the type of tissue involved and climatic or seasonal variations in bacterial flora.

Recently, a new factor, epidemiologic in nature, that appears to be related to the use of antibiotics has been introduced—namely, the dissemination of drug-resistant bacteria. It is my purpose to discuss this man-made phenomenon and to present data indicating, paradoxically, that the use of antibacterial agents may unfavorably influence the postoperative infection rate. If such an effect is eventually proved efforts toward achievement of excellence in surgical and antiseptic technics will need redoubling, for the prevention of crosscontamination appears to be the only solution to the problem.

This report deals with the incidence of postoperative sepsis in so-called clean wounds and with the staphylococcal carrier rate in hospital patients and personnel. The discussion does not encompass the influence of the other important factors already mentioned.

Reports from various laboratories throughout the world[4-9] bear out the fact that penicillin-resistant strains of coagulase-positive hemolytic *Staphylococcus aureus* recovered from hospitalized patients have increased since the introduction of penicillin in 1941. Earlier reports indicated that resistant strains were found in only about 10 to 15 per cent of those tested whereas more recent studies show that 50 to 75 per cent of staphylococci from various clinics are penicillin resistant.[4,5,10-12] There are a number of articles in the literature describing therapeutic failures as a result of infection with penicillin-resistant *Staph. aureus*,[4,5,11,13] but these reports are as yet few in view of what might be anticipated from the emphasis on the laboratory findings. Various mechanisms have been postulated for the development of resistance,[14,15] but most investigators have stressed the fact that all resistant strains of staphylococci isolated from their patients have been penicillinase producers. This type of resistance is not an acquired characteristic. Recent studies,[16,17] which have included bacteriophage typing of strains, indicate that the widespread use of penicillin has reduced the number of sensitive strains and allowed penicillinase-producing staphylococci to flourish and become predominant. These resistant strains are then disseminated from patients to carriers and thence to other patients. Spread probably occurs largely by personal contact, as emphasized by Miles,[18] but Clarke et al.[16] recovered resistant staphylococci from ward air and dust, the number of organisms recovered correlating roughly with the amounts of antibiotics used on a given ward. There has evidently been a change in the type of bacterial population, rather than an actual development of resistance under treatment in most cases so that penicillinase-producing staphylococci, formerly in the minority, have now become predominant in certain areas. It appears that to maintain a high incidence of resistant strains among carriers, a large number of patients must be receiving the drug.[19] This condition is fulfilled on a surgical service where many patients are receiving penicillin, the most commonly used antibiotic, therapeutically and prophylactically.

It is apparent that this increase in the number of resistant strains is observed primarily in hospitals. This is attested by the following facts: the greatest prevalence of resistant organisms is found in hospital patients, among whom penicillin is most heavily used; the number of resistant strains isolated from outpatients is roughly half that isolated from inpatients; and present information does not indicate that naturally occurring staphylococci carried by the population at large are frequently resistant to penicillin.

It is also apparent from recent studies that staphylococcal resistance, whatever the mechanism may be, is likely to develop with other antibiotics than penicillin and that the development of resistance to a drug is roughly in proportion to its use in a given area. The

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resistance pattern of a bacterial species, therefore, may vary from time to time in an institution, depending, among other things, on the antibiotic being used most extensively.

Recent articles[20,21] have stressed the relatively high concentration of resistant micrococci among hospital populations as compared to normal subjects, and Lepper et al.[19] have called attention to the importance of carriers among hospital personnel as a means of cross-contamination. These authors report an increase from 0 to 75 per cent of erythromycin-resistant staphylococci among workers in their institution during a five-month period when the drug was employed more frequently than any other in the treatment of patients. The percentage fell to 35 per cent after the use of erythromycin was discontinued. Concurrent with the rise in carrier rate the incidence of resistant strains infecting the trachea of tracheotomized patients increased from 0 to 95 per cent in a three-month period.

An awareness of these factors, together with personal experience and discussions with various surgeons, suggested that postoperative clean-wound sepsis due to *Micrococcus pyogenes* var. *aureus* (*Staph. aureus*) is probably on the increase, at least in some hospitals. Early in 1953 an epidemic of these infections on the wards of the Massachusetts Memorial Hospitals led to a survey of the problem at this institution. The results of preliminary observations seem worth reporting and indicate not only that infection due to *Staph. aureus* is widespread but also that there has been a progressive rise in the over-all frequency of postoperative wound infections. There is reason to believe that similar surveys in other institutions would show comparable findings. On a well regulated surgical service the rate of wound infections should not exceed 1 or 2 per cent of the clean operations. Because of the relative infrequency of wound infection and the tendency for surgeons to minimize their poor results impressions are notoriously erroneous, and accurate statistics are required to present the true picture.

Materials and Methods

Frequency of Postoperative Sepsis

The data presented here were not collected during the course of a planned study, nor were the patients under research control. Statistics were compiled in retrospect by a review of all operations performed during the years 1949 to 1953, inclusive, on the general surgical service, both house and private. Records were crosschecked with the weekly surgical-staff-meeting reports on complications and with the reports of cultures submitted to the bacteriologic laboratory. Operations were classified as follows:

Group A. Clean operations such as herniorrhaphy, mastectomy and sympathectomy.

Group B. Operations in which there is actual or potential contamination but in which wounds are normally expected to heal by primary intention, such as cholecystectomy, intestinal resection, perineal surgery and skin grafting of an ulcer.

Group C. Operations in which sepsis is expected or obligatory — for example, drainage of an abscess.

Group D. Other procedures, not involving incisions, such as reduction of a fracture and endoscopy.

Group A and B operations are considered "clean" for purposes of this report. Infections are classified as major (serious) if they caused systemic manifestation, progressive invasion or destruction of tissue or prolongation of the hospital stay or if there was induced or spontaneous drainage of pus requiring therapy. They are classified as minor (trivial) if they showed only localized inflammatory reaction in skin margins, stitch abscesses or a trivial localized area of sepsis. Special study sheets were compiled from each septic case recording the type and duration of operation, the names of the surgeon, assistants and scrub nurses, the type of preoperative skin preparation, suture technic and material, drainage, type of anesthesia, data on seasonal incidence, nutritional state of the patient, bacterial flora of infected wounds and sensitivity of the organisms to antibiotics. Tables were constructed from these sheets.

Carrier Rate of Hospital Patients and Personnel

It is known that the nose and nasopharynx are the chief reservoirs of virulent staphylococci[18,22] and that nasal carriers or patients with open wounds containing this organism also carry it on the skin very frequently.[23]

The patients and personnel on one ward (house service) and in the operating room were chosen as a sample cross-section on which to perform a cursory check of the hospital carrier rate of *Staph. aureus*. In August, 1953, cultures on all patients, house officers, nurses, orderlies, dietitians, clerks, messengers and all persons working in the selected areas on both day and night shifts were performed. Swabs wet with beef-heart infusion broth enriched with sheep's blood and fortified with para-aminobenzoic acid were used to culture the nose and nasopharynx, and another swab was drawn across the length of the hand and down each finger — that is, five times each on both dorsal and palmar surfaces. Cultures were planted in beef broth and on blood-agar plates.

All floras were tested for sensitivity by means of antibiotic disks* containing 1 unit of penicillin. The disks were placed on blood-agar plates freshly inoculated directly from the culture swabs, and the zones of inhibition were interpreted after twenty-four hours' incubation at 37°C. Particular attention was given to the size of the inoculum. If the plate did not

*Dia-Discs, available from Commercial Solvents Corporation, New York City.

present a solid sheet of growth the test was repeated with a heavy inoculum. Pure subcultures of staphylococci were made for sensitivity testing in a few cases when necessary because of the presence of other bacteria. Organisms with zones of inhibition of 11 mm. in diameter or less were considered resistant to penicillin. All others were considered penicillin susceptible for the purposes of this survey.

Results

Postoperative Sepsis in Clean Wounds

Table 1 shows that the total rate for major and minor infections in 1949 was 1.09 per cent of the clean operations but that there was a gradual stepwise increase to 3.98 per cent in 1953. This occurred despite the widespread prophylactic use of antibiotics. As in most institutions the infection rate for house-service cases was considerably higher than that for private ones but it can be seen that both increased in proportion over the five-year period. Except for the adoption of new refinements in preoperative and postoperative care as they appeared on the surgical scene no innovations in surgical or therapeutic technics were inaugurated during the time covered by this study. In recognition of the fact that surgeons are encountering geriatric problems more frequently as the life span is increased, the nutritional status of all patients was classified on the basis of age, weight, blood chemical and hematologic studies and the clinical statements in the record; there was no significant difference in the clinical status between 1949 and 1953. Correlation charts failed to identify any person or technic as a common source of contamination. A slight spring and summer increase during 1949-1951 tended to disappear during 1952-1953 as the infection rate became higher.

Table 2 shows that the greater portion of the wound infections were major or serious and that the same year-by-year increase prevailed as in the over-all percentage. These data are supplemented by Table 3, which gives the percentages for minor wound infections. There was an apparent increase for house cases in 1952-1953, but the frequency of minor wound sepsis in private patients remained essentially unchanged throughout the five years.

These results were examined by Mr. John Alman, director of the Office of Statistical Research Services of Boston University. After applying chi-square analysis, supplemented by variance analysis using the square-root transformation[24-26] to the data in Tables 1 and 2, he concluded that the yearly increases in wound infection were significant in terms of percentage rates. The rate of infection was thus higher in house-service cases than in private ones, and showed a significant increase over the past five years. Construction of the Poisson index of dispersion for the figures in Table 3 showed that the apparent increase in minor infections for house cases in 1952-1953 was not statistically significant. The statistical evi-

TABLE 1. *Rates of Major and Minor Wound Infections after Group A and B (Clean) Operations.**

SAMPLE STUDIED	1949		1950		1951		1952		1953	
	NO. OF OPERATIONS	INFECTIONS %	NO. OF OPERATIONS	INFECTIONS %	NO. OF OPERATIONS	INFECTIONS %	NO. OF OPERATIONS	INFECTIONS %	NO. OF OPERATIONS	INFECTIONS %
House service	401	1.99	379	3.16	366	3.82	388	5.15	429	7.22
Private service	796	0.63	750	1.06	843	1.18	805	1.24	800	2.25
Totals	1197		1129		1209		1193		1229	
Averages		1.09		1.77		1.98		2.51		3.98

*Note gradual, stepwise increase since 1949, in spite of widespread use of antibiotics prophylactically. Yearly percentage-rate increases are statistically significant.

TABLE 2. *Percentages of Major Wound Infection after Group A and B (Clean) Operations.**

YEAR	INFECTIONS ON HOUSE SERVICE	INFECTIONS ON PRIVATE SERVICE	AVERAGES
	%	%	%
1949	1.24	0.25	0.58
1950	2.10	0.53	1.06
1951	3.00	0.71	1.41
1952	3.09	0.99	1.68
1953	4.66	1.87	2.85

*Almost all increase in clean-wound infections, depicted in Table 1, due to major or serious sepsis. Same stepwise increase apparent and highly significant when subjected to statistical analysis.

TABLE 3. *Minor Wound Infections after Class A and B (Clean) Operations.**

YEAR	INFECTIONS ON HOUSE SERVICE	INFECTIONS ON PRIVATE SERVICE	AVERAGES
	%	%	%
1949	0.75	0.38	0.50
1950	1.05	0.53	0.71
1951	0.81	0.47	0.58
1952	2.06	0.24	0.84
1953	2.56	0.37	1.14

*Data supplementary to those in Table 2. Statistical analysis showed that no significance could be attached to apparent increase in minor wound infections for house-service cases in 1952-53.

dence regarding minor wound infections was inconclusive, and no further analysis can be made until at least another year has been added to the series. It

TABLE 4. *Occurrence of* Staph. aureus *in Flora of Major Wound Infections Cultured from Patients on Private and House Services.*

YEAR	OCCURRENCE IN FLORA		OCCURRENCE AS PREDOMINANT ORGANISM	
	RATIO	PERCENTAGE	RATIO	PERCENTAGE
1949	6:7	85.7	4:7	57.1
1950	10:12	83.3	7:12	50.8
1951	12:17	70.6	7:17	41.2
1952	13:17	77.6	10:17	58.8
1953*	30:31	96.8	25:31	80.6

*Although both ratio to flora and rate of occurrence as predominant organism were high in 1953 analysis showed no statistical evidence of significant yearly change.

therefore seems that the yearly increase in rate was almost entirely due to major wound infections.

The occurrence of *Staph. aureus* in the major wound infections is shown in the left-hand column of Table 4. In 1949 there were 7 major wound infections, and this organism was present as a component of the flora in 6 of them, or a rate of 85.7 per cent. In 1953, on the other hand, 30 of the 31 major infections cultured contained *Staph. aureus* — a rate of 96.8 per cent. In the right-hand column of Table 4 the data are presented in a different way — namely, the number of times in which this micro-

TABLE 5. *Penicillin Sensitivity of* Staph. aureus *Recovered from 55 Major Wound Infections in 1952-53.**

DATUM	NO. OF CASES
Culture performed	48
Staph. aureus found	43
Test for penicillin sensitivity	31
Penicillin-resistant *Staph. aureus* found	29
Penicillin-sensitive *Staph. aureus* found	2

*Although not all cultures tested for penicillin sensitivity, great majority of those tested penicillin resistant.

coccus was either the predominant or the responsible organism. *Staph. aureus* was the sole or predominant organism in 4 of the 7 infections in 1949 whereas in 1953 it was responsible for 25 of the 31 infections — the rate increasing from 57.1 to 80.6 per cent. An obvious objection to the material in Table 4 is the relatively small number of infections in 1949 as compared with those in 1953. Indeed, chi-square analysis both for total occurrence and frequency as predominant organism showed no statistical evidence of a yearly increase. The material is therefore not being presented as statistical proof of increase but as the only information available regarding yearly incidence.

The data on penicillin sensitivity of strains recovered from major wound infections are unsatisfactory because susceptibility tests were not done on a number of the cultures. Before 1952 such testing was not commonly performed on this service except on a research basis. Table 5 shows that, in 1952-1953, 43 of the 48 major infections cultured yielded *Staph. aureus*, that 31 were tested for penicillin sensitivity and that 29 of these were resistant and 2 sensitive.

Carrier Survey in Patients and Personnel

Eighty-eight personnel and 37 patients were cultured. Of these, 124, or 99.2 per cent, carried *Staph.*

TABLE 6. *Staphylococcal Survey of Nose, Nasopharynx and Hand-Skin Cultures.**

DATUM	NO. OF CASES
Culture on personnel	88
Culture on patients	37
Total	125
Staph. aureus carrier	124(99.2%)
Nose carrier	116
Hand carrier	100

*Practically all patients and personnel carried *Staph. aureus* in nose or skin, and most carried it in both areas.

aureus either in the nose or nasopharynx or on the skin, and the majority had the organism in both areas (Table 6). Since the nose and nasopharynx are the most important reservoir, the organisms recovered from nasal cultures were subjected to penicillin sensitivity tests (Table 7). Of 116 strains, 91, or 78.5 per cent, proved to be penicillin resistant. The highest incidence of heavy growth occurred in personnel having most intimate contact with patients — namely, nurses, aides and attendants. Doctors were next in

TABLE 7. *Penicillin-Resistant Strains among Carriers.**

DATUM	NO. OF CASES
Nasopharyngeal carriers	116
Penicillin-resistant *Staph. aureus*	91(78.5%)
Penicillin-sensitive *Staph. aureus*	22(19.0%)
Unsatisfactory test	3(2.5%)

*Over three quarters of strains carried penicillin resistant.

frequency, and personnel having relatively little actual patient contact demonstrated lighter growth on culture. Anesthetists yielded uniformly heavy growth.

DISCUSSION

Most reports identify *Staph. aureus* as the commonest wound pathogen, especially in war wounds.[22] Melency[1] found it in 46 per cent of major clean-wound infections over an eight-year period. In the present survey the rate of 96.8 per cent in 1953 appears to have been quite high even though it could not

be statistically demonstrated to have increased over the past five years. Such a high rate suggests that *Staph. aureus* is assuming a more important role as a cause of clean-wound sepsis.

There is no way of determining the carrier rate at this institution in the prepenicillin era. We cannot, therefore, conclude categorically that it has increased. In the literature, however, there are a number of excellent surveys on the rates of nasal and skin carriers of *Staph. aureus* in hospital personnel before the days of antibiotics. These data, which have been summarized by Miles et al.,[27] are presented in Table 8. It can be seen that the rate of nasal carriers ranged from 22 to 45 per cent in various institutions before 1941, whereas Tables 6 and 7 indicate that in the present survey nearly 100 per cent of the sample were carriers; three quarters of these strains were penicillin resistant. A comparison of these figures with those from other institutions is, of course, not statistically valid but suggests that the carrier rate in the present survey was abnormally high at the time it was made. If this experience is the same as that reported from other hospitals, and there is a great likelihood that it is, it appears that the rate was not always as high as it is now but that it has increased in recent years.

Several factors, then, support the hypothesis that the widespread use of penicillin in this hospital has resulted in an increased infection rate owing largely to penicillin-resistant *Staph. aureus*. In the first place there is the statistically valid evidence that the over-all rate has increased significantly during the last five years almost entirely because of major wound infections. Secondly, the carrier and wound-infection rates for *Staph. aureus* in the hospital are high; there is a suspicion that both have increased although the data at hand do not allow the conclusion that they have done so during the last five years. Thirdly, penicillin-susceptibility data show that the majority of strains tested were resistant. Lastly, reports from this country and abroad agree that penicillin-resistant strains of *Staph. aureus* recovered from hospital patients are on the increase. It is likely that the rise in the number of such strains is true in this hospital and in many others where there have been large numbers of patients and extensive use of penicillin over the years. The increasing number of resistant staphylococci might be expected to have as discernible an impact on surgical wounds as it has in the field of medical infections, in which therapeutic failures, superinfections and crosscontamination problems have recently been reported.

Under the circumstances described it is easy to explain a high rate of infections due to the staphylococcus but perhaps more difficult to explain the rise in the total number of infections. It seems unlikely that there has been a progressive increase in the number of exposures or breaks in technic over the past five years. Is there something about a penicillin-resistant staphylococcus that causes it to be more virulent and likely to colonize when seeded into a wound? A possible explanation for the over-all increase in infection rate is that some of the normal constituents of the respiratory flora are nonpathogenic organisms for wounds, whereas others of low virulence may be destroyed by the normal defenses of the body when inoculated into a wound; still others, such as the hemolytic streptococcus, are penicillin sensitive and do not become resistant. Penicillinase-producing, resistant *Staph. aureus,* on the other hand, is a hardy wound pathogen, with invasive, hemolytic and necrotizing properties, that tends to colonize in tremendous

TABLE 8. *Rates of Nasal and Skin Carriers Reported in the Literature (Adults, Not Clinically Infected).**

SOURCE	NO. OF CASES	CARRIER RATE†		
		TOTAL NOSE	TOTAL SKIN	NOSE & SKIN
		%	%	%
Hallman (1937)	158	39.0	—	—
McFarlan (1938)	132	35.0	—	—
Devenish and Miles (1939)	40	45.0	5.0	2.5
Gillespie et al. (1939)	159	43.0	20.0	13.0
Vierthaler (1940)	100	—	21.0	—
Bartley (1941)	82	22.0	21.0	6.0
Smith (1941)	100	32.0	5.0	4.0
Martin (1942)	100	—	24.0	—
Present series	479	47.4	18.4	11.7

*Based on Miles et al.[27]
†Determined on hospital staffs, hospital patients and medical students.

numbers and to become ensconced in impermeable foci surrounded by necrotic tissue.[28] In a hospital ward, where penicillin is freely used, there are usually one or more open wounds containing this organism. Personnel are constantly exposed to dressings, dust from sweeping, bed making and so forth, and their noses, nasopharynges and skin are likely to become carrier sites for pathogenic staphylococci that are added in varying numbers to the normal flora. A patient with an open wound on the ward or in the operating room has no greater chance than formerly of becoming contaminated; the important difference lies in the type and preponderance of the contaminating organisms almost universally carried by the personnel. This sequence of events may well explain the over-all increase in wound sepsis and also may account partially for the higher rate of sepsis in house-service patients. For, in addition to his inexperience, the surgical house officer spends much of his time in the hospital, where, because of the nature of his duties, he has great opportunity of coming in contact with these resistant organisms. He is, therefore, more likely to become a "heavy" carrier than the visiting surgeon, who spends relatively few hours in the hospital. Private operations, moreover,

are likely to be shorter, and the patients are apt to be in single rooms and hence less susceptible to cross-contamination than those in the wards.

This problem is important both medically and financially. The findings discussed above cast additional doubt on the wisdom and efficacy of routine prophylactic systemic antibiotic therapy in clean surgery. It is difficult to find scientific justification for its use in the literature. It will mask and delay the appearance of wound infection but apparently will not prevent it. This delay is no doubt beneficial in military surgery, but the disadvantages of routine systemic prophylaxis outweigh the possible benefits when applied to clean uncomplicated surgery in civilian practice. Much time and expense will be saved by the restriction of antibiotics to the early treatment of established infection in the few cases in which it does follow clean operations. The possible tendency to use chemotherapy as a partial substitute for meticulous sterile technic will also be avoided. There are a number of other reasons for which prophylaxis is advocated — for example, the prevention of pulmonary complications; again, however, the evidence in its favor is certainly not clear cut[29] and there is further need for controlled study of this problem. The picture as a whole must be considered before any type of prophylaxis is fully condemned. There is, however, a healthy skepticism and a growing reluctance to use prophylactic antibiotics routinely for clean surgical operations in many institutions. It is not to be inferred that abolition of prophylactic antibacterial treatment would solve the problem because the indicated therapeutic uses in hospitals would probably be sufficient to perpetuate a certain number of resistant strains. Nevertheless, the indiscriminate administration of antibiotics should be discouraged and prophylaxis and multiple drugs should be avoided except when they are known to be clearly indicated and beneficial.

It is beyond the scope of this paper to discuss the treatment of these infections, once established, or to describe preventive measures. A definite program to lower the rate of wound infection has been inaugurated in this hospital, consisting mainly of numerous measures to prevent crosscontamination. Isolation technics were found to be impractical. Because the nasopharynx is the main carrier site for the staphylococcus double masking is considered important. Surgeons and nurses are urged to wear masks and gloves for all contaminated dressings *mainly for self protection to help prevent the carrier state.* Vigilance in aseptic technic in the operating room and on the ward is emphasized. Probably the most important factor in prevention is an awareness on the part of the staff of the nature, magnitude and epidemiology of the problem. There are as yet too few new cases on which to base any conclusions, and seasonal variation may profoundly effect results unless at least a year is taken into account.

Summary and Conclusions

A review of the literature indicates that penicillin-resistant strains of *Staphylococcus aureus* recovered from hospitalized patients and personnel have greatly increased throughout the world since the introduction of penicillin in 1941. Therapeutic failures as a result of infection with penicillin-resistant *Staph. aureus* are becoming more common. It is evident that penicillinase-producing coagulase-positive *Micrococcus pyogenes* (var. *aureus)* is the responsible organism in most cases and that the rate of nasal and skin carriers of this organism in hospital personnel is extraordinarily high.

Data are presented showing that the rate of infections of clean wounds after operation at the Massachusetts Memorial Hospitals has gradually increased in a stepwise, statistically significant fashion over the past five years despite the prophylactic use of antibiotics. Analysis of the hospital carrier rate and bacterial flora of infected wounds strongly suggests that this increase in postoperative sepsis is due to an abnormally high penicillin-resistant carrier rate in hospital personnel and patients as a result of the widespread use of penicillin. There is reason to believe that similar situations exist in other institutions. These findings are in keeping with the recognized trend toward increase in the number of penicillin-resistant staphylococci being reported and the clinical and therapeutic problems that result from it in the field of medical infections. The serious physical and financial burdens imposed on patients who contract major postoperative sepsis merit continued study along these lines by surgical groups.

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SICKLE-CELL TRAIT AND SPLENIC INFARCTION ASSOCIATED WITH HIGH-ALTITUDE FLYING*

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THE danger of high-altitude flying to patients with sicklemia, until lately, has been more theoretical than real. As recently as 1951 Margolies[1] said that "the sickle cell trait is not a contraindication to high altitude flying." This statement was based principally on studies by Henderson and Thornell[2] and Findlay, Boulter and MacGibbon,[3] as well as on the fact that few published reports linked sickle-cell crisis with airplane flights.

Sullivan[4] (1950) described a young sicklemic patient who apparently had episodes of splenic infarction after each of two airplane flights over the Rocky Mountains; this was regarded as a chance occurrence. Recently, however, Cooley et al.[5] showed that the triad of sickle-cell trait, flying and splenic infarction is not a rare one. In describing 6 additional cases at a single Air Force base — 4 occurring within two months — these authors have demonstrated the consistency of the clinical picture. Two additional cases with similar histories have been observed by Van Avery.[6] In each of the cases reported the patient was a young Negro serviceman who within two hours of high-altitude flying had nausea, vomiting and persistent pain in the left upper quadrant. Examination revealed striking left-upper-quadrant tenderness, frequent splenomegaly and decreased to absent bowel sounds. Laboratory data indicated an increase in neutrophils, a slightly decreased hemoglobin and a positive sickle-cell preparation (Table 1). Those authors emphasized that splenectomy was the treatment of choice.

Table 1. *Clinical and Laboratory Data.*

Source	Race	Age	Flight Time at Onset	Fever	Nausea & Vomiting	Left-Upper-Quadrant Pain	Splenomegaly	Bowel Sounds	Admission White-Cell Count	Neutrophils	Hemoglobin	Sickling Preparation
			hr.						*x 10³*	*%*	*gm./100 cc.*	
Sullivan[4]	N	18	1±	Absent	Present	Present	Present	—	19.4	80	14.5	+
Cooley et al.[5] (Case 1)	N	22	2±	Present	Present	Present	Absent	Depressed	15.3	86	11.9	+
Cooley et al.[5] (Case 2)	N	18	2±	Present	Present	Present	Absent	Normal	—	—	—	+
Cooley et al.[5] (Case 3)	N	23	<½	Present	Present	Present	Present	Normal	11.0	89	8.0	+
Cooley et al.[5] (Case 4)	N	21	<½	Present	Present	Present	Absent	Depressed	8.5	75	16.4	+
Cooley et al.[5] (Case 5)	N	23	1±	Present	Present	Present	Present	Normal	18.8	95	14.0	+
Cooley et al.[5] (Case 6)	N	21	4±	Present	Present	Present	Present	Depressed	24.3	90	11.9	+*
Present report (Case 1)	N	22	2±	Present	Absent	Present	Absent	Normal	19.1	80	14.5	+
Present report (Case 2)	N	22	2±	Present	Absent	Present	Absent	Normal	21.0	85	15.5	+

*Positive on pathological specimen.

*From the Medical Service of the United States Army Hospital, Camp Kilmer, New Jersey.

†Formerly, James Hudson Brown Fellow, Yale University School of Medicine.

The purpose of this paper is to report 2 additional cases of this syndrome and to show that in these cases conservative medical management was entirely satisfactory.

Case Reports

Case 1.§ A 22-year-old Negro sergeant was admitted to the Medical Service of the United States Army Hospital, Camp Kilmer, New Jersey, on July 18, 1953. His chief complaint was pain in the left lower part of the chest and the left upper quadrant of the abdomen. This patient, who had just returned from combat in Korea, had been in the best of health when he boarded a plane to fly eastward from San Francisco. After flying for about 90 minutes he noted the gradual onset of a moderately severe pleuritic type of pain in the left lower portion of the chest anteriorly. He continued on to New York in spite of the pain and remained there for 2 days before appearing at this medical installation. During this time the chest pain persisted, and fever developed, without other symptoms. Although he had flown several times previously he had never before had an illness resembling this one. There had been no associated gastrointestinal complaints. He had never been known to be anemic, and his weight had been stable for several years.

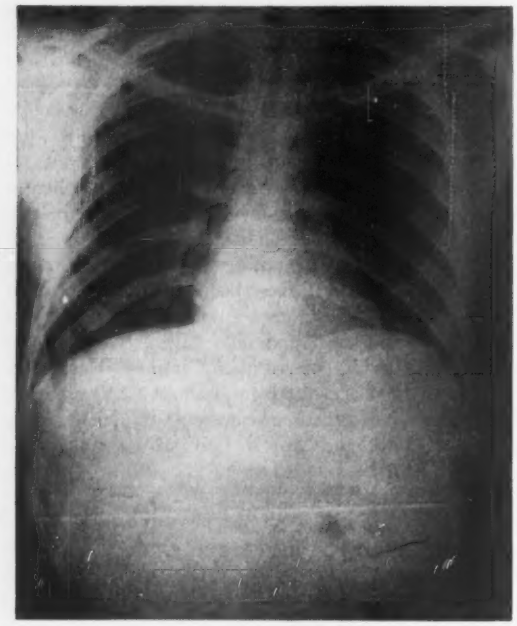

Figure 1. *Roentgenogram of the Chest in Case 1 Taken Five Days after Admission, Showing Elevation of the Left Leaf of the Diaphragm.*

The past medical history and system review were nonrevealing. The patient had previously enjoyed remarkably good health. At 8 years of age he had had a "sore" on his left shin that had taken a long time to heal.

The family history was noncontributory. No relatives had had anemia, jaundice or leg ulcers to his knowledge.

Physical examination disclosed a man who appeared acutely ill and apprehensive. The skin was hot and dry. The neck was supple. The conjunctivas appeared slightly pale, but there was no scleral icterus. The fundi did not show any abnormal vascular tortuosity. The ears, nose and throat demonstrated only dryness of the membranes. The trachea was in the midline. There was splinting of the left side of the chest on inspiration. At the left base, posteriorly, there seemed to be some dullness with decreased resonance and occasional rales. The diaphragm, however, moved with respiration. The abdomen was normal except for left-upper-quadrant tenderness, but the spleen was not palpable. The remainder of the physical examination was negative except for the presence of a 2-cm., circular, atrophic scar on the anterior aspect of the left leg.

The temperature was 101°F., the pulse 120, and the respirations 18.

Examination of the blood revealed a hemoglobin of 14.5 gm. per 100 cc. and a white-cell count of 19,000, with 80 per cent neutrophils and 18 per cent lymphocytes. The urine gave a + test for albumin. A serologic test for syphilis and malaria smears were negative. Roentgenograms of the chest were normal. Urine, blood and sputum cultures were of no help.

As the symptoms and fever persisted, many laboratory studies were performed. Multiple sputum examinations for the tubercle bacillus were negative, as were agglutination tests for typhoid, paratyphoid, brucellosis and tularemia. Cold-agglutination tests, heterophil-antibody tests and liver-function tests (including bilirubin, cephalin flocculation, thymol turbidity and alkaline phosphatase) were negative, as were the serum amylase and lipase. An electrocardiogram was normal. Five days after admission the left leaf of the diaphragm was found to be elevated on a chest roentgenogram although it moved fluoroscopically (Fig. 1). Sickle-cell preparations at this time showed 25 per cent sickled erythrocytes.

For more than 2 weeks after admission the patient had a daily temperature elevation of 101 to 103°F. Although he continued to have pleuritic pain on the left he did not appear critically ill. During this period the hemoglobin fell to 12.0 gm. per 100 cc. A pleural friction rub on the left was heard on the 10th and 11th hospital days. At this time oxytetracycline, 2 gm. a day, was given empirically. Lysis of fever, which started 6 days later, was apparently unrelated to the antibiotic. Simultaneously, the symptoms disappeared, and the white-cell count fell to normal. The spleen had never been palpable and did not seem enlarged on a roentgenogram of the abdomen.

Case 2.§ A 22-year-old Negro sergeant was admitted to the hospital on July 17, 1953, complaining of pain in the left side of the chest and upper abdomen. The patient, who had just finished a tour of active duty in Korea, first noted the pain while flying eastward from San Francisco. The pain, which appeared after he had been flying for about 2 hours, became more severe and knifelike, and at the 1st intermediate landing he noted that it was aggravated by both coughing and deep inspiration. It continued unabated until he reached this post and was admitted to the hospital. He had been in excellent health during his Korean service and had felt well when he boarded the plane. He was not aware of fever or chills and had experienced no gastrointestinal complaints. There was no history of cough, night sweats, hemoptysis, weight loss or known exposure to tuberculosis.

The past medical history and review of the systems were noncontributory. The patient had always been in good health. He had not had any operations or severe injuries. He had never had anemia, jaundice or skin ulcers.

The family history was equally unrevealing. No one in the family had had anemia, jaundice, leg ulcers or tuberculosis.

Physical examination revealed a man who seemed to be in acute distress, with left-upper-quadrant pain and slight dyspnea. There was no scleral icterus. The fundi showed normal vascular arrangement. The head, neck, ears, nose and throat were not remarkable. The heart was of normal size and displayed normal sinus rhythm without murmurs. There was minimal limitation of motion of the left side of the chest. The lungs were clear to auscultation and percussion. The abdomen was soft, but with voluntary spasm and diffuse tenderness, most marked in the left upper quadrant. The spleen could not be felt. There was slight left-costovertebral-angle tenderness. There were no scars on the lower extremities. Neurologic examination was negative. The skin was warm but had good turgor.

The temperature was 100.4°F., the pulse 94, and the respirations 16. The blood pressure was 114/65.

Examination of the blood disclosed a red-cell count of

§Dr. Ernest W. Smith has recently studied the hemoglobin pattern by means of paper electrophoresis and has confirmed the diagnosis of sickle-cell trait.

4,900,000, with a hemoglobin of 15.5 gm. per 100 cc., and a white-cell count of 21,000, with 85 per cent neutrophils. The sedimentation rate was 19 mm. per hour, corrected. Urinalysis was normal except for a +++ test for albumin and 6 to 8 white blood cells per high-power field in the sediment. A serologic test for syphilis was negative. A roentgenogram of the chest was normal. Three days later x-ray study showed a small pleural effusion on the left (Fig. 2). The cardiac silhouette and pulmonary parenchyma were normal. Fluoroscopic examination was not performed.

The patient was treated with mild analgesics and empirically received 600,000 units of penicillin twice each day. He had an unremittent low-grade fever for approximately 1 week, after which the temperature dropped to normal. The discomfort lasted for several days and then gradually disappeared. Because of the great similarity to Case 1 a sickle-cell preparation was examined, and it showed 5 to 10 per cent sickling in 2 hours. Subsequent preparations performed 1 month later were negative. The white-cell count fell to normal as the patient's condition improved. Simultaneously the pleural effusion disappeared. Tuberculin tests in 1st and 2d strength were negative.

The patient was followed for a full month without further symptoms of any sort.

Discussion

The occurrence of the sickle-cell trait has been reported in about 8 or 9 per cent of American Negroes.[1,7] Approximately 1 in 40 of these show the full-blown picture of sickle-cell anemia.[1,7,8] During World War II, when flying became almost a military necessity for very large numbers of men, Henderson and Thornell[2] investigated the effect of lowered oxygen tension on American Negroes with sickle-cell disease by use of a low-pressure chamber simulating high-altitude flight. They were unable to show any evidence of intravascular sickling or hemolysis in their volunteers with the sickle-cell trait. One subject with sickle-cell anemia had more sickling as the oxygen tension decreased, with return toward normal after the inhalation of oxygen. During an actual flight Findlay, Boulter and MacGibbon[3] had confirmed these findings in West African Negroes with this condition. It was concluded that the possibility that sickle-cell crisis was precipitated by flying was not a real one, but the prophylactic use of oxygen was suggested.

The first case of this chain of events was reported in 1950 by Sullivan.[4] This single report was regarded as a bizarre case, but indicated that some precautions might be wise to prevent further occurrences. The recent study by Cooley et al.[5] has shown beyond question that the lowered oxygen tension of high-altitude flying, in patients with the sickle-cell trait, can produce a sharply defined syndrome. The 2 cases reported above bring to 9 the total of such cases.

Although the exact altitude and the level of pressure in the cabin at the time of the onset of symptoms is not known in any of these cases, it is significant that it occurred after flying over the Rocky Mountains in 7 of the 8 cases. The eighth case occurred during flight from southern Texas to Francis E. Warren Air Force Base near Cheyenne, Wyoming, which itself is over 6000 feet above sea level. One may thus speculate on the predisposing factors necessary for this syndrome. It has been shown that reduced oxygen tension is conducive to intravascular sickling.[9,10] It is also known that all sickle-cell patients do not respond equally to the same reduction of oxygen tension, nor does the same patient react equally to the same stimulus at all times.[2,3,11] The rarity of this condition may then be explained by the theory that this complication would occur only in patients with the greatest sensitivity to the oxygen lack, at a given time, during flights at the more extreme altitudes. The effect of

Figure 2. *Roentgenogram of the Chest in Case 2 Taken Three Days after Admission, Showing Left-Sided Pleural Effusion.*

the relative percentages of sickle-cell or other abnormal hemoglobins that make up the patient's red cells remains to be determined.

It has been shown in a number of studies that patients with sickle-cell anemia characteristically have splenic infarcts.[1,6,12] In fact the common finding of minute spleens, or "autosplenectomy," in sickle-cell anemia has been considered to be due to fibrous contraction of multiple thromboses of splenic vessels.[1] It is consequently unusual to find splenomegaly in adults with sickle-cell anemia. It appears, therefore, that the patient with sickle-cell anemia is able to survive multiple episodes of splenic infarction without surgical intervention.

Similarly, the treatment of bland splenic infarcts has usually been expectant and symptomatic regardless of the etiology of the condition. Neither Lahey and Norcross[13] nor Cole et al.[14] mention splenic infarct as an indication for splenectomy. Krumbhaar[15] believes that "surgical intervention is not required un-

less chills and septic fever indicate the formation of abscesses."

It may thus be concluded that the treatment of choice in cases of bland splenic infarcts in sickle-cell anemia is conservative medical management. However, if during the period of medical observation complications of progressive severity develop, as in the first case of Cooley et al.,[5] exploratory laparotomy is mandatory. The presence of leukocytosis and nonseptic type of low-grade fever are the rule (Table 1), and by themselves do not constitute an indication for surgery. It must also be emphasized that this syndrome in the presence of a *negative* sickle-cell preparation, as occurred in 3 cases reported,[5] presents a somewhat different picture, and one that almost demands surgical exploration.

Since all 11 cases of splenic infarction precipitated by high-altitude flying have occurred in military personnel, it would undoubtedly be advantageous to the armed forces to initiate a program to prevent such occurrences. The program might include the routine sickle-cell testing[16] of all Negroes on induction, to be performed along with the routine serologic test for syphilis. The results of the positive tests might easily be included in the patient's official records and on his identification tag. All men with the sickle-cell trait would then use surface transportation exclusively during their military careers. The availability of emergency oxygen tanks on all military aircraft would allow prophylactic oxygen administration to such men when aerial movement is mandatory, as might occur in the air evacuation of wounded. Indoctrination of these men in the inherent dangers of high-altitude flight would help decrease this hazard. Such precautions could almost completely eliminate the occurrence of this syndrome.

Summary

Two more cases of splenic infarction in Negroes with the sickle-cell trait, precipitated by high-altitude flying, are presented.

The literature on this syndrome is reviewed, and a well defined symptom complex is recognized.

The treatment of these cases is considered to be conservative medical management, with splenectomy only upon the development of complications.

A general program for prevention in the armed forces is proposed.

Motulsky[17] recently reported an additional case of this syndrome that followed a flight over the Rocky Mountains. He found by filter-paper electrophoresis that the patient's hemoglobin contained both sickle-type hemoglobin and C hemoglobin.

Dr. C. L. Conley, in a personal communication, has informed me that he is aware of 9 additional cases not reported in the literature.

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EXTRAPROSTATIC FACTORS IN URINARY RETENTION*

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ENLARGEMENT of the prostate is so preponderantly the major cause of urinary retention and its surgical treatment has been so generally successful that it may mask other disturbances of bladder function. The development of retention in patients who show no obstruction at the vesical orifice or its persistence in those who have been subjected to prostatectomy, with apparently adequate indication, suggests that other factors are operating, either alone or in combination with enlargement of the gland. Obviously, these factors must be recognized and evaluated if unnecessary surgery is to be avoided, and satisfactory functional results assured in patients for whom operative intervention is indicated.

The lower urinary tract is not a lifeless conduit, but a delicately adjusted mechanism, and micturition is a dynamic function. Retention of urine results from an imperfect adjustment between two forces, the pro-

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pulsive power of the detrusor muscle of the bladder and the resistance offered at the bladder neck and in the posterior urethra. To these may be added the further possibility of obstruction by stricture in the more distal part of the urethra. In a somewhat oversimplified form, this may be expressed as follows: failure of propulsive force from neurogenic or structural causes; obstruction of the bladder neck and posterior urethra (because of prostatic enlargement, such conditions as contractures and median bar and congenital lesions) and strictures of the distal urethra; or a combination of these causes.

When combinations of these factors occur they are often interrelated. Primary neurogenic dysfunction, for example, is almost always followed by significant structural alterations. More pertinent to the present discussion is the association of prostatic enlargement with other elements of dysfunction, which may be either coincidental or the result of long-standing obstruction.

Failure to achieve good functional results after prostatectomy have, naturally enough, focused attention upon organic obstructive sequelae of the operation itself — remnants of tissue, strictures, membranes, false passages and the like. Brodny and Robins[1] have demonstrated such lesions by careful urethrocystographic studies on a large series of patients. It has repeatedly been observed, however, that some patients in whom no such obstructions can be recognized nevertheless cannot satisfactorily empty their bladders after operation. In a study covering almost 15,000 patients who had had prostatectomies of various types[2] 2.8 per cent were found to have persistent residual urine without demonstrable obstructive lesions.

The following are the disorders that most commonly contribute to dysfunction, in association with prostatic enlargement or other obstruction at the bladder neck: stricture of the distal urethra; coincidental detrusor dysfunction; detrusor dysfunction resulting from obstruction (reversible or irreversible).

Stricture

Pre-existing stricture, as distinct from that which complicates surgery, may be missed during the original investigation. Attention is usually focused on the prostatic obstruction, and since catheterization in such cases is frequently attended with some difficulty anyway, the presence of a second obstructing lesion, distal to the prostatic urethra, may be overlooked. Further urethral manipulations carried on in the course of the usual diagnostic studies or the presence of an indwelling catheter may serve to dilate it so that it becomes even less evident. It will almost certainly be picked up if a transurethral operation is undertaken, but if open operation is performed, it may not manifest itself for some weeks. A careful calibration of the urethra, including urethrography, should therefore be carried out on every patient, however obvious the fact that he is suffering primarily from obstruction at the bladder neck. If a stricture is found it should be adequately treated — dilatation at suitable intervals is usually all that is required — before and after the surgical intervention. Exact figures are not available, but the association of stricture, usually of gonorrheal origin, with bladder-neck obstruction is by no means uncommon.

Detrusor Dysfunction

Dysfunction of the detrusor, resulting in inadequate propulsive force, may be coincident with obstruction at the bladder neck although in no way related to it etiologically. Usually, it is of neurogenic origin, with tabes dorsalis, diabetes and multiple sclerosis often in the background. In any given case, however, there may be no other evidence of organic disease of the nervous system. Cystometric studies should therefore be a routine part of the investigation of all patients with any type of micturitional disturbance, since they may reveal evidence of detrusor inadequacy complicating an obvious obstruction. A careful neurologic examination should be done and, in doubtful cases, examination of the spinal fluid. The cystogram ordinarily shows a large, smooth, overdistended bladder (Fig. 1), as in the following case:

Figure 1. *Atonic Bladder of Undetermined Cause before Operation in Case 1.*

Case 1. A 56-year-old man was admitted to the hospital with moderate hematuria and symptoms of mild cystitis. On cystoscopic examination a small ulcer was found on the dome of the bladder, biopsy of which revealed no evidence

of cancer. The patient had no obstructive symptoms and no endoscopic evidence of obstruction at this time. The original diagnosis was abacterial cystitis, and he responded well to the usual treatment with Mapharsen.

After discharge he was examined at intervals of 2 or 3 months, the biopsy being repeated several times and cytologic studies of the urine carried out frequently. During this period a histologic diagnosis of cystitis cystica was established; he remained comfortable and symptom free. Eighteen months after the 1st admission he returned with a recurrence of hematuria and mild obstructive symptoms. On this occasion he was found to have a residual urine of 1000 cc. and cystometric studies revealed almost complete atony of the bladder. There was still no evidence of obstruction at the bladder neck. Neurologic examination was negative, and the spinal fluid showed no abnormalities. A partial cystectomy was performed, approximately two thirds of the wall of the bladder being removed. This disclosed atrophy of the muscle bundles, which were widely separated by fibrotic edematous tissue. There was little or no cellular reaction and no evidence of cancer. The mucosal lining had been reduced to a single layer of transitional cells, with occasional cystic nests of cells close to the surface, characteristic of cystitis glandularis. The diagnosis was a severe atrophy of the bladder wall, nonspecific in character and of unknown etiology.

FIGURE 2. *Cystogram in Case 1, Three Months after Partial Cystectomy.*

The patient did very well after operation, and was discharged in good condition and with a residual urine of only 15 cc. Figure 2 shows the postoperative cystogram. He returned a few months later complaining of difficulty in voiding, and some urgency. His residual urine at this time varied between 200 and 240 cc. Cystoscopic examination revealed a slight degree of bladder-neck contracture, and a transurethral resection was accordingly performed, only a few grams of tissue being removed. The patient made an uneventful recovery and since then has been voiding normally and with no residual urine. Cystometric studies made a year after the transurethral resection showed approximately normal tonus.

In this case the cause of the changes in the bladder wall could not be specifically determined. It is possible that they were the result of purely local disturbance in the form of chronic cystitis. Of more interest, perhaps, than the exact cause of the detrusor dysfunction is the fact that although it may not have been etiologically related to the subsequent contracture of the bladder neck, there was an obvious functional interrelation. Both factors had to be treated to obtain a good result.

OBSTRUCTION

From a practical clinical point of view the most important group of patients, and the largest, comprises those in whom the functional inadequacy of the bladder muscle is a result of long-standing obstruction, leading to chronic overdistention and usually infection. This was recognized and described as long ago as 1911.[3] In 1948 Crabtree and Muellner[4] suggested partial cystectomy as a means of restoring function when the changes in the bladder wall had reached an irreversible stage. The lesion they described, found also by various other observers, as well as in the cases on which this study is based, consisted largely of scarring of the detrusor, with a considerable increase in the amount of fibrous tissue between the muscle bundles, giving the impression of islands of good muscle surrounded by scar. Such a bladder is large, with a capacity of as much as 2000 or 3000 cc. When emptied, it characteristically does not contract smoothly, but collapses upon itself in large, thick folds. The method of treatment by excision of the redundant portion of the bladder has been successfully utilized by others.[5] It should be borne in mind that these changes need not reach an irreversible stage. In a sense, functional decompensation of the detrusor may be said to exist whenever there is residual urine. In most cases, however, removal of the obstructive lesion is in itself sufficient treatment, and the bladder wall is capable of a prompt resumption of its normal activities. A consideration of the character of the structural alteration may help to clarify this phenomenon. The first response of the bladder wall to obstruction is hypertrophy, and, up to a point, this may provide adequate functional compensation. Eventually, as the degree of obstruction increases, the propulsive force becomes insufficient. Infection, moreover, almost invariably supervenes. The result is chronic cystitis and scarring, which further diminish the effective contractility of the detrusor. Chronic overdistention leads to further injury and more scarring, with the ultimate result already described in terms of the histologic findings. It is obvious that if the obstruction can be eliminated while the bladder muscle still possesses the capacity to function without this impediment, the condition may be considered reversible. Nesbit[6] has pointed out the great importance of recognizing any serious degree of decompensation before operation is undertaken, emphasizing

that prompt drainage rather than early prostatectomy is indicated in such cases. During drainage, the function may be checked from time to time by cystometry or cystography. If, as in some cases, azotemia is present, this period will provide an opportunity for the improvement of the patient's general condition and, in particular, of his kidney function.

There is no precise measure of the degree of improvement in detrusor function to be expected before surgical treatment of the obstruction is undertaken. In this connection, however, there is an interesting phenomenon that has not been emphasized in the literature. Even when a static level of function has been reached during catheter drainage, surgical removal of the obstruction may lead to further improvement. An attempt to explain this is perhaps beyond the province of the present discussion, but it is apparent that the presence of an indwelling catheter is a deterrent to complete function of the bladder. Chronic low-grade infection, an inevitable accompaniment of continued drainage, is probably another factor.

In any event, once the situation has been thoroughly investigated, it is probably justifiable to go ahead with the removal of the obstruction as soon as the patient's general condition warrants. If, after recovery from operation, the function remains inadequate, conservative measures may be undertaken with a greater chance of success than before. The most important of these is habit training. In essence this is a remarkably simple approach, but its effectiveness is frequently impaired by the unwillingness or inability of the patient to co-operate and by the fact that its results are gradual rather than dramatic. Physiologically, however, it is entirely sound. It should be instituted as soon as there is evidence that, in spite of the removal of the obstruction, the bladder is not emptying itself adequately. Continuous drainage for a few days is the first step; tidal drainage is an excellent means of conditioning the detrusor, and an aid in improving bladder hygiene. The catheter is then removed, and the patient started on a schedule of regular voiding at fairly frequent intervals, usually beginning with one hour. The fluid intake may be so adjusted that by voiding just before retiring, and being called once or twice during the night, he can avoid nocturnal overdistention. It has been observed in these patients with diminished detrusor function that a bladder that can successfully contract down upon and expel a reasonable content — for example, 240 to 270 cc. — may be unable to do so if distended beyond this point. Furthermore, the changes in the bladder wall may have so impaired the sensory innervation that the patient does not become aware that his bladder is filling, until it has actually reached a stage of overdistention, at which it can no longer operate efficiently. He may then void a reasonable quantity but carry as a residuum as much urine as he has passed. Voluntary emptying of the bladder at regular intervals avoids this chronic overdistention and permits the detrusor to become conditioned to a reasonable load. As time passes, the interval between voidings can be gradually increased until an optimum is reached. These men may be reminded that, during the development of obstruction, they might have fallen into the habit of voiding only at long intervals; it must be explained that satisfactory function can be maintained only if these intervals are reduced. The majority can be trained so that they need void no more often than every three hours and not at all or, at most, only once during the night. During the early days of this training, the cholinergic drugs are sometimes of value, particularly when there is some sensory impairment. Acting directly through the parasympathetic efferent innervation, they may replace the absent afferent stimuli in the reflex arc. Urecholine, in doses of 10 mg. two or three times a day, has occasionally been useful in such cases. Its administration is seldom required for longer than two or three days.

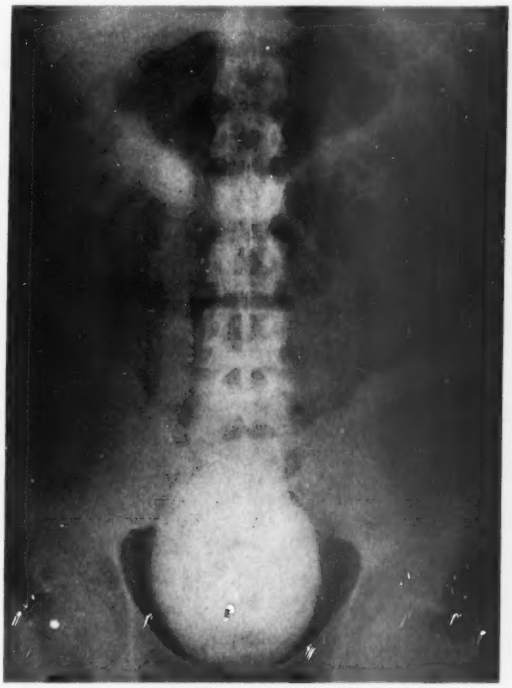

FIGURE 3. *Atonic Bladder in Case 2, with Congenital Contracture of the Bladder Neck, Showing Also Bilateral Vesicoureteral Reflux.*

In the following case, in a bladder that eventually recovered good function after removal of the obstruction, without further surgery, vesicoureteral reflux had already developed bilaterally, with hydroureter and hydronephrosis. The essential lesion was a moderate degree of congenital contracture at the bladder neck (Fig. 3):

CASE 2. A 32-year-old man was admitted to the hospital with acute pyelonephritis, one of a series of similar episodes

that had rendered him practically an invalid for several years. His residual urine was 800 cc., although he apparently voided with no great difficulty. Since this was a congenital lesion the bladder had apparently adjusted itself to a state of considerable distention, and there was no such trabeculation as is usually seen with chronic obstruction. A cystometrogram showed the usual almost complete atony. Constant drainage was begun, and the patient treated medically for the pyelonephritis, with marked improvement of the general condition. In spite of drainage there was no improvement in detrusor function. It seemed almost inevitable that removal of the redundant portion of the bladder would be required, but since there was a known obstructive lesion, it was considered that this should be handled first. Accordingly, a transurethral resection was done, the tissue removed showing chronic inflammation and some fibrosis.

FIGURE 4. *Intravenous Pyelogram in Case 2 after Transurethral Resection, Showing Improvement in the Upper Urinary Tract.*
There was no reflux at this time.

The patient made a good postoperative recovery and was put on bladder training as already described. The residual urine a few days after removal of the catheter was 70 cc. He was discharged under close observation; there was still considerable doubt whether or not the detrusor could continue satisfactory function. A cystogram taken 4 months after operation revealed a bladder of slightly larger than normal size, but with no evidence of vesicoureteral reflux. An intravenous pyelogram taken at about this time (Fig. 4) demonstrated great improvement in the status of the kidneys and ureters. The patient was in excellent health, had had no recurrence of upper-urinary-tract infection and was working regularly. Voiding was normal; the bladder capacity was 300 cc., and the residual urine 60 cc. Judging from past experience in similar cases, he will probably continue without further trouble, illustrating the impressive capacity of the detrusor to resume effective functional activity even after a long period of insult. Incidentally, this patient demonstrated, as the next case did, the serious effect of neglected bladder obstruction on the upper urinary tract.

In the following case the structure of the bladder had become so seriously altered that adequate emptying was impossible, even after removal of the obstructing prostate gland:

CASE 3. A 58-year-old man was admitted to the hospital with complete retention, with 2000 cc. of urine in the bladder. He had been told 8 years before that he needed a prostatectomy, but he refused operation at that time. He was in generally poor condition, with hypertensive cardiovascular disease and moderate uremia. Cystometric examination showed almost complete atony, and a cystogram demonstrated a large and slightly irregular bladder. Studies of the upper tract indicated considerable diminution of renal function, with a huge bilateral hydroureter and hydronephrosis. The patient was put on catheter drainage, which was continued for 3 weeks, with moderate improvement in his general condition but no specific alterations in the detrusor function. A suprapubic prostatectomy was then done, and he made a fairly good recovery except for a transitory ileus. By the time the wound had healed and the catheter was out, the blood nonprotein nitrogen had fallen but had not yet reached normal; the general condition was much better and voiding seemed normal, but there was a residual urine of 300 cc. Since it was considered desirable to avoid further surgery, if possible, and since he felt better than he had in years, he was sent home, under close observation, to see whether or not improvement might be achieved by careful habit training. This, unfortunately, was unsuccessful and he returned to the hospital with the residuum still at 300 cc. A period of tidal drainage, followed by more efforts at habit training and the administration of urecholine, failed to effect any change. A partial cystectomy was done, and after recovery the residual urine fell to 60 cc. During the next few months, on follow-up examinations, the residual urine varied between 30 and 60 cc., the urine was clear, and the blood nonprotein nitrogen fell to normal. The patient remained in excellent condition until about 4 months after operation when homologous serum jaundice developed. He recovered from this, however, and when last seen, 2 months later, was in excellent condition, with a residual urine of 0.

CONCLUSIONS

Patients with prostatic enlargement and other types of obstruction at the bladder neck may have concomitant disturbances that contribute significantly to the micturitional dysfunction. One of these is preexisting stricture of the distal urethra.

Decompensation of the detrusor may exist coincidentally with the obstruction, although etiologically independent of it. This may be a result of a structural or a purely functional deficiency, or both. This type of dysfunction may be corrected, in some cases, by the elimination of the associated obstruction.

A more important type of dysfunction results from the alterations in the wall of the bladder that develop in consequence of long-standing obstruction. These may be reversible to the degree that they do not prevent the resumption of normal function after operative removal of the obstructing factor. A satisfactory result, however, may require careful conservative management after operation, with particular attention to habit training.

These alterations are sometimes irreversible in the sense that, after removal of the obstruction, satisfactory function is not restored by any methods short of further surgical intervention. This usually takes the form of a partial cystectomy, the redundant portion of the bladder wall being removed.

In every patient presenting a disorder of micturition, even when an obstruction is obvious, careful evaluation should be made of all the factors involved in micturitional function. This will be of aid in the charting of a suitable course of preoperative and postoperative treatment. The investigations involved — cystometry, cystography and frequent checking of the residual urine — are simple, safe and inexpensive.

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CHRONIC CONSTRICTIVE PERICARDITIS AS A SEQUEL TO ACUTE BENIGN PERICARDITIS*

Report of a Case

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ACUTE benign pericarditis is a well recognized clinical syndrome, but its relation to chronic constrictive pericarditis is still a matter of dispute. Pathological studies of autopsy and operative material obtained from patients with constrictive pericarditis have shown some variation in the etiology, but in all the series reported, a large percentage of cases have been placed in the group with no specific cause (Table 1). There is evidence that many of these cases are the end result of so-called acute benign pericarditis. The case reported below represents typical acute pericarditis with massive effusion that failed to respond to medical management. The patient was treated surgically and found to have an underlying constrictive pericarditis.

TABLE 1. *Causes of Constrictive Pericarditis.*

Source	Total No. of Cases	Idiopathic Cases	Cases Due To Tuberculosis	Cases Due To Rheumatic Heart Disease	Miscellaneous Causes
		%	%	%	%
Chamblis et al.[1]	61	37.7	28.2	1.6	12.5
Kaltman et al.[2]	18	55.5	11.1	27.9	5.5
Moschcowitz[3]	130	25.5	3.1	46.2	25.2

Case Report

T.B. (M.H.X8707), a 40-year-old man, entered the hospital on June 23, 1952, with the chief complaint of substernal pressure and fever. He had been well until 1 week before admission, when he suddenly experienced shortness of breath and substernal pressure.

System review and family history were entirely noncontributory. There was no previous upper respiratory infection and no history of hypertension, rheumatic fever or tuberculosis. He visited his family physician, who found marked enlargement of the heart and referred him for admission.

Physical examination showed a well nourished, well developed man in no acute distress. The ocular fundi and pupils were normal. The pharynx was normal. The neck veins were greatly distended in the erect position and filled from below. The lungs revealed dullness and bronchovesicular breathing below the angle of the scapula on the left. On percussion the heart was found to be considerably enlarged, the border extending to the left and right. The heart sounds were regular and extremely distant. No murmurs or adventitious sounds were heard. The liver edge was palpable 1 fingerbreadth below the right costal margin in the midclavicular line. There was no peripheral edema. All pulses were palpable, and pulsus paradoxicus was obtained. An x-ray film brought by the patient disclosed great enlargement of the heart. There was no evidence of pulmonary tuberculosis.

The temperature was 100.4°F., the pulse 84, and the respirations 20. The blood pressure was 140/100 in the right and 150/100 in the left arm.

The venous pressure on admission was 240 mm. of water. The circulation time with Decholin (arm-to-tongue method) was 18 seconds. Repeated urinalyses were negative. Examination of the blood demonstrated a red-cell count of 5,000,000, with a hemoglobin of 15 gm. per 100 cc., and a white-cell count of 9500 with a normal differential. The blood sedimentation rate (Wintrobe method) was 12 mm. per hour. The blood Mazzini test was negative. Fasting blood sugar, urea nitrogen, total protein and albumin-globulin ratio were normal. Two L.E.-cell preparations from the peripheral blood were negative. The antistreptolysin titer was less than 100 units per cubic centimeter. The uptake of radioactive iodine was 22 per cent after 24 hours. Three pericardial taps were done, the fluid after each being yellow and nonclotting, with a specific gravity of 1.020. Microscopical examination revealed 4 or 5 lymphocytes per cubic millimeter. The protein content was 5 gm., 2.5 gm.

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and 6 gm. per 100 cc. on 3 determinations. Cultures for all organisms, including acid-fast bacilli, were negative, and cell-block examinations showed no neoplastic cells. The Mantoux test was negative up to 1:100 dilution. Cold and heterophil-antibody agglutinins were not found. Electrocardiograms disclosed low voltages throughout and right-axis deviation (Fig. 1). X-ray examinations on admission and 2 weeks later were identical, showing striking enlargement of the cardiac shadow (Fig. 2*A*).

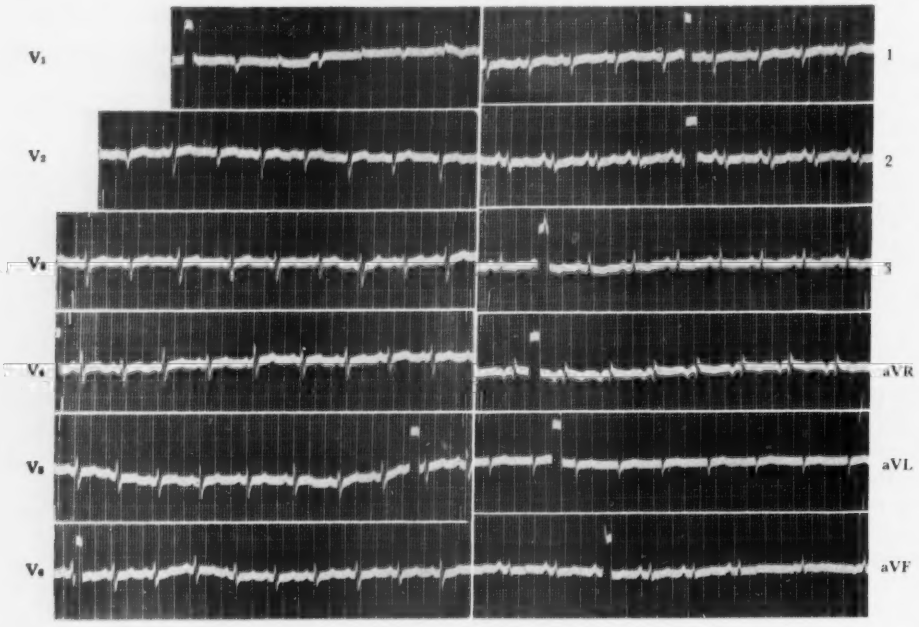
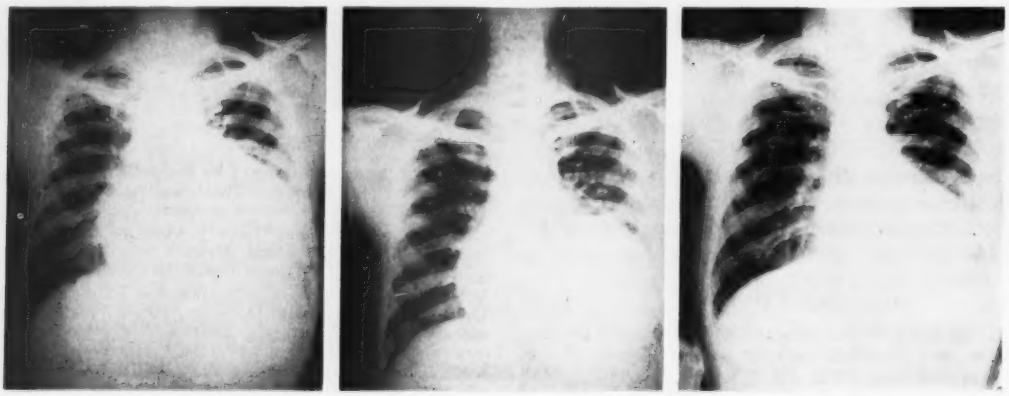


FIGURE 1. *Electrocardiogram on Admission.*

associated with an episode of pneumonitis. The patient was asymptomatic throughout except for episodes of mild orthopnea. Pain was not a prominent feature of the illness. On the 17th and 24th hospital days pericardial paracenteses were done in the 5th interspace, left mammary line, without incident; 300 and 550 cc. of clear, yellow fluid were obtained, and 75 and 100 cc. of air were injected for purposes of x-ray identification (1,200,000 units of penicillin was administered intramuscularly each time). There was a rapid fall and



A B C

FIGURE 2. *Films of the Chest Taken at Various Times during the Course of the Illness.*

The hospital course can be followed in Figure 3, in which the venous pressures are charted. Circulation times with Decholin (arm-to-tongue method) paralleled the venous pressures, as did the enlargement of the liver and the neck-vein distention. Eight days after admission the temperature reached normal and remained so except for an elevation then a rise in venous pressure after these procedures (Fig. 3).

X-ray examination immediately after the 2nd paracentesis demonstrated a pleural effusion on the left side, suggesting that some of the pericardial fluid had run off into the left pleural space. An air bubble was noted along the left upper

part of the cardiac silhouette, delineating the pericardium (Fig. 2*B*). The x-ray film showed no diminution in size of the cardiac silhouette despite the removal of 550 cc. of fluid.

On August 7, when the venous pressure was 250 mm. of water, and paracentesis was done again, 600 cc. of clear,

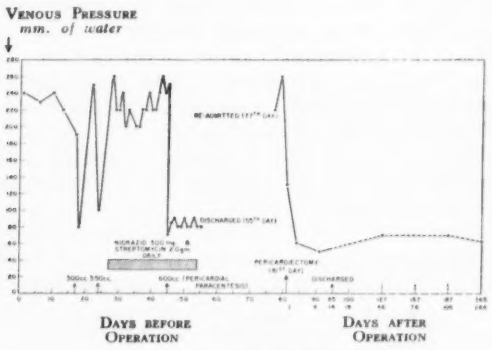


Figure 3. *Hospital Course.*

straw-colored fluid was removed. The venous pressure dropped to 77 mm. of water immediately and remained in the range of 80 to 90 mm. to the end of the hospital stay on August 25, when the patient was discharged to remain under observation at home. In the hospital mercurial diuretics and penicillin had been given, and on July 21 nidrazid, 300 mg. daily, and streptomycin, 2 gm. daily, were begun. This was continued until August 18. No benefit was observed from any medication.

The patient felt well during his stay at home. Examination 11 days after discharge from the hospital revealed prominence of the neck veins. Fluoroscopic examination showed the cardiac silhouette to be undiminished in size. The venous pressure was 220 mm. of water.

He was readmitted to the hospital for pericardiectomy on September 10. The liver edge was felt 5 fingerbreadths below the right costal margin. The venous pressure was 258 mm. of water, and the circulation time 29 seconds. An electrocardiogram was practically identical with the last tracing taken during the 1st hospital admission (Fig. 4). On September 12 (3 months after the onset of illness) a pericardiectomy was performed.

A transverse anterior thoracotomy was done through the right and left 4th intercostal spaces. After aspiration of the pericardial effusion the anterior portion of the parietal pericardium was completely excised, the posterior line of resection being just posterior to the phrenic nerve, which was spared. The heart was compressed by a thickened, whitish visceral pericardium, and the excursion of both ventricles was less than normal. The epicardium was elevated bluntly as a thin fibromembranous sheet from the surface of the myocardium, and was stripped in this manner from the anterior surface of the right atrium and great veins, and from the anterior, posterior and inferior surfaces of the right and left ventricles, care being taken to avoid the coronary vessels.

After excision of the visceral pericardium the heart action was dramatically improved, and both ventricles expanded and contracted in normal fashion. The pulse pressure immediately increased from 20 to 40. The procedure was well tolerated, and the patient returned to the ward in good condition.

The pathological report was as follows:

Microscopical sections reveal granulation and loose and dense connective tissues with considerable discrete and coalesced mononuclear-cell infiltrations. Specific structural alterations are not found.

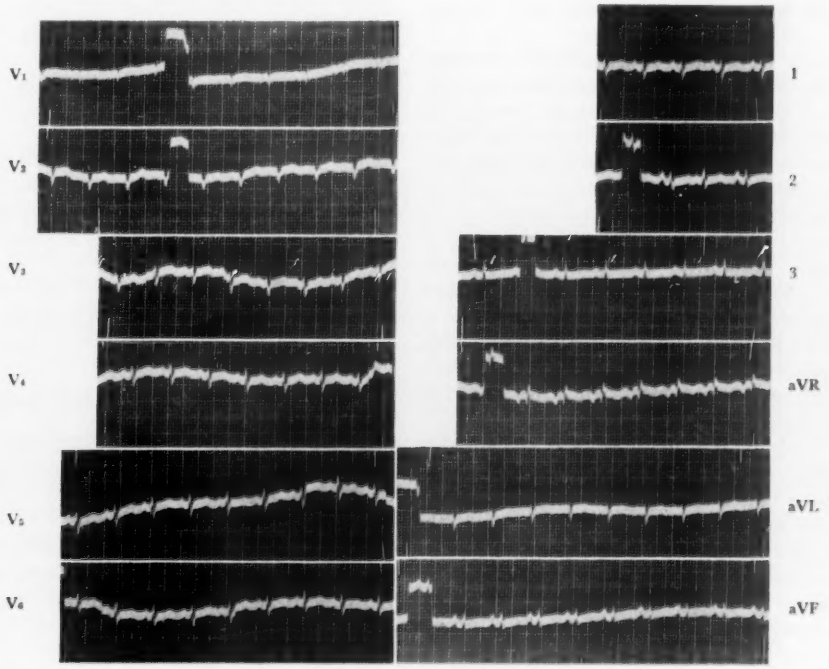


Figure 4. *Electrocardiogram before Operation.*

After operation all determinations of venous pressure were normal. X-ray study of the chest 3 months later (Fig. 2*C*) demonstrated diminution in size of the cardiac silhouette although the heart remained slightly enlarged.

Eighteen months after operation the patient was asymp-

tomatic, had gained 20 pounds and had returned to work and full physical activity. The liver was no longer palpable. However, on fluoroscopic examination, the heart continued to be slightly enlarged.

Discussion

The presence of an underlying constricting visceral pericardium was not suspected preoperatively. Pericardiectomy was performed for the following reasons: we were dealing with a pericardial effusion of unknown etiology that showed no tendency to subside spontaneously despite 3 pericardial paracenteses and various types of medications; and there was evidence of circulatory embarrassment in the prominent neck veins, high venous pressure, liver enlargement, pleural effusion and occasional orthopnea. We feared the development of irreversible myocardial and hepatic damage.

There is ample evidence that prolonged elevation of venous pressure may cause visceral damage. Godfrey[4] reported 3 cases typical of acute, nonspecific pericarditis with evidence of residual myocardial damage long after the initial acute pericarditis had subsided. He concluded that acute nonspecific pericarditis may be followed by prolonged or permanent myocardial injury.

Moschcowitz[3] postulated that persistent high venous pressure could cause phlebosclerosis. He pointed out that sclerosis of the hepatic veins was found in every one of his patients with constrictive pericarditis. He also noted congestive splenomegaly, cardiac sclerosis and sclerosis of the pulmonary capillaries indicative of pulmonary hypertension.

From a review of the literature it is evident that the therapeutic results of pericardiectomy are generally good and that the surgical mortality of this operative procedure is low (Table 2). Technically, the operation of pericardiectomy is performed with greater ease if attempted early in the course of the disease. The epicardium can then be separated easily from the myocardium, whereas the development of fibrous adhesions between the pericardium and epicardium in the later stages of the disease can make this procedure difficult and hazardous.

Summary and Conclusions

A typical case of acute benign pericarditis with massive effusion is presented. Because of failure to respond to conservative measures the patient was treated surgically and found to have an underlying constrictive pericarditis. Investigation failed to demonstrate any definite etiologic agent.

This case demonstrates a possible etiologic relation between acute benign pericarditis and chronic constrictive pericarditis.

Table 2. *Therapeutic Results of Pericardiectomy.*

Source	No. of Cases	Operative and Postoperative Deaths	Patients Greatly Improved	Patients Moderately Improved	Patients Unimproved
Chambliss et al.[1]	61	11(18%)	38(62%)	6(10%)	6±(10%)
Evans et al.[5]	30	3(10%)	18(60%)	7(23%)	2±(7%)

Because permanent visceral damage may occur in long-standing cases of constrictive pericarditis and because of the technical ease of operation in the subacute phase of the disease, early operation is recommended in any patient who fails to respond to conservative management with a prompt and sustained drop in venous pressure.

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SPECIAL ARTICLE

THE ROTTERDAM PORT DEMONSTRATION CENTRE*

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IT is common knowledge that in recent years rapid strides have been made in the fight against venereal diseases, especially as a result of new remedies, including the antibiotics. For another reason the number of cases of infection is smaller today than formerly. Recourse to prostitutes — formerly looked upon as a normal procedure in certain sections of the community — is nowadays disapproved, at least in this part of the world.

This development, however, must not lead to an overoptimistic judgment. As recently reported, a number of the members of the American Academy of Dermatology and Syphilology, who met in Chicago in December, 1953, thought that the time had come to drop the "and Syphilology" from the title of the organization.

> **Before the week was well along, the specialists changed their minds. Syphilis, they heard, had gone down for a count of nine but is now up and swinging again. Reported Dr. John C. Cutler of the U. S. Public Health Service: in the last fiscal year, 15 states and the District of Columbia have reported increases in the number of cases of syphilis. . . . We are still faced with a tremendous problem . . . of approximately 2,100,000 cases of untreated or inadequately treated syphilis.‡**

Venereal diseases have so far stubbornly persisted, especially in one section of the population — the seamen. Even here, it is true, there has been a decline in the number of cases, but the improvement cannot be compared with that recorded in other sections. It stands to reason that, by the nature of his calling, the seaman is particularly exposed to these diseases, and for the same reason it is difficult to ensure effective treatment for him. Thus, the Danish dermatologist, G. Hartmann, who studied the cases of syphilis and reported his findings to the Public Health Service of Copenhagen in 1952, found that the seamen played an important part in the problem in Denmark. Of the total of 103 cases of primary and secondary syphilis in the Copenhagen material about 33 per cent were due to "import," and, of these cases, 73.5 per cent could be traced back to seamen, Danish and foreign in about equal proportions.

Experts are convinced that this problem can be solved only by systematic, co-ordinated measures.

This view was molded by an American physician, J. R. Heller, Jr., into a concrete and original plan, which, in October, 1947, he submitted to a meeting of the International Union against Venereal Diseases in Paris. The gist of this plan was the proposal that a demonstration project be set up in a European port. For this purpose a port was to be chosen where the fight against venereal disease among seamen was already being waged systematically and on all fronts — not only, therefore, on the medical but also on the sociomedical and social fronts and not only by therapeutic but also by preventive measures. These activities were to be made the subject of investigation and study, so that, on the basis of the experience gained, a scientific composite of the methods of fighting venereal disease among seamen might be devised that could be made use of elsewhere.

These suggestions were received with general approval. The interest of the World Health Organization was brought out in full relief by the idea that, after the investigation, courses should be arranged during which the results of the investigation and study could be laid before doctors and social workers from other seafaring countries. This plan was rightly regarded as the best means of letting a number of countries share in the fruits of the investigation and of promoting in those countries, as far as desirable, a speedy realization of the ideas and views obtained.

CHOICE OF LOCATION

It is not necessary here to relate, step by step, the further history of the plan. Suffice it to say that the World Health Organization soon decided to grant technical and financial aid and as a first step in the realization of the plan to designate Rotterdam as the Project Port.

Rotterdam was chosen for this honor because of its favorable situation at the mouth of the Rhine, with the intensive traffic of both seagoing and river craft, which ensured a sufficient number of patients to enable the study of the disease in question to be made. In addition the Central Organization for Skin and Venereal Disease Control was in operation there under the skillful and active leadership of Dr. E. H. Hermans, Sr. The esteem felt in international circles of experts for the work done by Dr. Hermans and the fact that the center under his care offered ample accommodation for both therapeutic and pedagogic purposes were also factors in the choice of Rotterdam. Also, there are in Rotterdam social institutions for seamen, such as seamen's houses, an

*A co-operative undertaking in maritime venereal-disease control sponsored jointly by the Government of the Netherlands, the Municipality of Rotterdam and the Central Organization for Skin and Venereal Disease Control at Rotterdam, with the technical assistance of the World Health Organization.

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‡*Time* 62:71 (December 21), 1953.

information service and a center for sport activities.

In joint deliberation among the Government, the World Health Organization, the Municipality of Rotterdam and the Central Organization for Skin and Venereal Disease Control, it was decided in 1951 to set up the Rotterdam Port Demonstration Centre. The conduct of the new establishment was placed in the hands of a steering committee of six; Dr. Hermans was appointed director.

Organization

Before the official opening took place much preparatory work had to be done. It was quite clear that a problem with many ramifications presented itself. Practice had already proved that a correct diagnosis, like treatment, presents many difficulties in this field, not only because the seaman is a professional traveler but also because of language barriers, short leaves ashore, unsatisfactory facilities for treatment in ports and insufficiently standardized methods of bacteriologic diagnosis, as a result of which the physician is often unable to decode a laboratory report made in the last place the seaman visited. Furthermore, it had appeared that in a serious effort to reduce venereal diseases attention must also be paid to the problem of prevention, especially social care and enlightenment.

For these reasons it was clear that the study that the new center was to undertake would obviously require the co-operation of many specialized experts. On closer examination it appeared that there were five distinct problems: the organization and running of treatment centers in the ports, in accordance with the relevant stipulations laid down by the so-called Brussels Convention; treatment both in port and on board ship; laboratory work, with attention especially directed to the standardization of bacteriologic methods; epidemiologic work (exchange of information on contacts, social and medical work, medical propaganda and so forth); and social care in a narrower sense (social measures on behalf of seamen, seen from both the sociopsychologic and the juridical points of view, seamen's houses and guidance).

For the investigation of these subjects five study groups of Dutch experts were set up. On the day on which the Demonstration Centre was officially opened, December 21, 1951, these groups began their work.

Many meetings have since been held, and the aid of experts from other countries has been repeatedly invoked. Several members of the groups paid visits to ports abroad. Dr. Hermans visited a number of ports in the Mediterranean. Numerous questionnaires were sent to ports all over the world. The final reports, which were ready in the autumn of 1952, were to serve as the basis for the courses after being discussed by the Steering Committee.

Report of Social Study Group

It is not intended to discuss all these reports here. An exception is made for the social report, not only because, as chairman of the Social Study Group, I know it best but also because the recognition of the social factor in this work is a feature of the contemporary scientific approach. As Dr. Hermans wrote in the program booklet of the first course:

> It is obvious that any determined effort to reduce the incidence of V.D. must go beyond medical and administrative measures to embrace, in the widest sense of the word, all the social and psychological aspects of the problem. The first international course at the Rotterdam Port Demonstration Centre must be considered in this light. By intelligent use of the latest methods of treatment, by the improvement of living conditions of seafarers, by properly educational coordinated international action it may be possible to eradicate venereal diseases, also among seafarers.

The recognition of the social factor in this work is a symptom of an attitude that is constantly gaining ground. In the sociomedical field this principle is expressed in teamwork for rehabilitation, psychosomatic medicine and medical research.

It is clear that a report on specific social measures on behalf of seamen must be based on a knowledge of the mode of life of the seafarer and the insight into his mental make-up. In other words, such a report must be based on a properly founded seafarer's sociology. The Study Group was promptly faced with the difficulty that special literature covering this field is practically nonexistent. Sociologic publications have already appeared covering different classes and professional groups, but the Study Group was able to find little literature about seamen. This meant that the Group, unlike the other study groups, from the beginning had no proper scientific basis on which to build. It had, therefore, first to set up that basis itself. This, of course, required much time and work.

The Group had to contend with another difficulty: the relative value of all social measures. The diagnosis of the different forms of venereal diseases can be made from the same symptoms in all parts of the world. Treatment can be carried out on the same principles and with the same pharmaceutical remedies. A good laboratory must meet the same minimum demands in Capetown and in Shanghai. Agreement can almost always be reached between reasonable people on the questions arising in these fields, because the relative effectiveness of ways and means can be verified objectively.

It is not such a simple matter with welfare work for seamen. A seamen's house offering cheer and comfort for Norwegians, Englishmen, Danes and Dutchmen does not necessarily appeal to Indonesians. One can please Norwegians, Englishmen and Swedes by arranging gymnastic events for them, whereas Turks and Spaniards are not attracted by this form of sport. Differences in religious conviction are also involved in this field.

It is clear that social work and recreation for seamen can succeed only if they are adapted to the cul-

tural and intellectual sphere from which the seamen come and in which they feel at home. Thus, in social endeavors, it is not always possible to recommend a particular working method as the only or the most suitable one. For that reason the Group endeavored in its report always to keep in view the relative value of its recommendations and to make them useful by basing them on the principle of diversity.

On the other hand general starting points in this work also had to be fixed. The reports, therefore, dealt in detail with the seaman's life on board, the isolation in which his work places him, the monotony of his surroundings and the character of the work performed by him. An effort was made to explain from these facts something of his mode of life, his attitude toward his family and his difficulties in general. On the basis of the views thus obtained the care of the seamen was discussed in the report. Attention was called, among other items, to the recommendations of the International Labor Conference at Geneva in 1936, which emphasized the necessity of good care of the health of seamen and recreation facilities both on board and on shore, as well as the importance of good seamen's homes, good lodgings and information centers. Limitations of space do not permit more than a mention of these points here.

The reports of the different groups have not yet been made public. They are at present no more than temporary working papers, which lecturers have used in the preparation of their discourses, and they have been continually discussed during the course as they will continue to be discussed in future courses. Later, they will probably be published in handbook form.

The first course has ended. It was held in English and lasted about three months, from September 21 to December 11. It was attended by 2 Germans, 1 Finn, 1 Spaniard, 1 Italian, 1 Frenchman, 1 Egyptian, 1 Sudanese, 2 Norwegians, 2 Swedes, 1 Yugoslavian, 1 Brazilian and 1 Iraqi. With the exception of the Swedish members — both female social workers — all taking part were dermatologists who, in their practices, had been and were still engaged in the fight against venereal disease among seamen.

In the beginning it was hoped that the attendance would be large, but early in the preparation of this course it became obvious that the World Health Organization, which had taken on the recruiting of the "Fellows," was up against serious difficulties. It appeared to be difficult to free doctors in the territories that would have derived most benefit from expert advice. Those familiar with the scarcity of physicians in the Middle East and in many districts of the Far East, the difficulty of finding a locum tenens and the lack of sufficient funds for this work will appreciate the magnitude of the problem.

All in all, those responsible for the course are not dissatisfied with the number participating. It is expected that the next course, which will be given in French, will be attended by a greater number.

Description of Course

First of all, for five weeks, a number of lectures were given by Dutch, English and some American and Norwegian experts. They covered the wide field of the Brussels Agreement and its application, health education, prostitution and its regulation, the organization of port centers and of a public-health service in ports and instruction of seamen regarding general hygiene and knowledge of venereal diseases. Laboratory diagnosis and clinical therapy of the various forms of venereal disease were discussed in detail; a number of lessons were devoted to the study of expressions in different languages for general use in clinic and hospital. Experience has shown that a knowledge of these terms is of the utmost importance to practicing port doctors and social workers.

On the average, lessons were given for four hours a day. They were varied by visits to institutions engaged in this department of public health.

The sixth and seventh weeks were taken up by a course at the laboratory in Utrecht and by a couple of short study trips to Belgium and Germany. The course in Utrecht dealt especially with laboratory research in syphilis (lectures, demonstrations and practical work), dark-field examination, serologic tests (complement-fixation tests), demonstration of preparation and preservation of antigens, complement, amboceptor and blood and demonstration of the Nelson test. The purpose of the study trips was to afford a knowledge of public-health organizations in port districts and visits to hospitals and venereal disease stations.

During the eighth week a study trip was made to Paris, where visits were paid to important institutions, among which the Institut Pasteur, the St. Lazare Hospital and the Alfred Fournier Institute are well known far beyond the frontiers of France.

The ninth week was chiefly devoted, again, to laboratory research, with lectures, demonstrations and practical work connected with it, and the following weeks were given over especially to the social and sociopsychologic aspects of the problem. In these lessons the medical and medicosocial work of the World Health Organization and the League of International Red Crosses in this field was discussed, in addition to all kinds of seamen's and boatmen's welfare work both in seaports and in river areas. Lectures were also given on seamen's mentality, psychiatric and social aspects of promiscuity and propaganda by posters, folders and so forth, and educational films were shown. Special attention was given to the influence of the physician's outlook on life and religious views on welfare work for seamen. Moreover, the wide field of recreative and pedagogic work

for seamen was considered in detail: on board ship, in seamen's houses and in private homes. Attention was also given to the seaman's family.

Discussion

This is a meager report of the many aspects of the course but sufficient, it is hoped, to give an impression of the great variety of the problems tackled. Naturally, certain weak spots in the organization have shown up. In the future a still more systematic division of the subject matter will be attempted. Experience has shown that field trips can be better spread over a longer period. Above all, only now are the proportions of the gaps in knowledge of the seaman and his life appreciated; this knowledge is indispensable to a really reliable and effective medical treatment. One result of the course is the idea of establishing in Rotterdam an institution where the most important questions regarding the seaman can be broadly studied.

Conclusions

The first course of the Rotterdam Port Demonstration Centre is considered to have been a success. The "Fellows" showed great and unflagging interest, which gave no signs of diminishing even toward the end. This is all the more important because the course included many subjects that do not belong to the everyday work of the port doctor.

Mention should be made of the excellent atmosphere prevailing among the participants during the entire course. The success must be attributed chiefly to the fact that it was possible to enlist the services of experts in their different lines. Also, the ability of the Director and his staff in the furtherance of good personal relations was of great value.

In the interests of both the many thousands of seamen sailing over the ocean and their families it is hoped that this realization of an American conception in the international field will fully come up to expectations.

MEDICAL PROGRESS

PERIPHERAL VASCULAR DISEASES (Concluded)*

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BOSTON

Diseases of Veins and Lymphatics

Varicose Veins

Many forms of mechanical obstruction and anatomic abnormalities have been blamed for simple varicose veins, but these factors have never been established as definite etiologic agents.[171,172] Heredity, it appears, plays the most important part, though a hormonal mechanism may also be involved during pregnancy. The symptomatology includes tiredness and heaviness of the legs, swelling, poor cosmetic appearance and ulceration. Even dyspnea, dizziness and precordial distress have been reported from pooling of blood in varicose veins.[169] It is possible frequently to outline the main and accessory venous trunks and also to determine the site of communicating veins feeding the varicosities by examination and by the Schwartz percussion maneuver.[172] Stripping of the long and short saphenous systems, along with any accessory venous trunks, is by far the most effective method of treating varicose veins.[168,170]

The use of large amounts of sclerosing solutions to obliterate these superficial veins frequently results in irreparable damage to the deep and communicating systems besides the discomfort produced; furthermore, subsequent stripping is made more difficult. However, a small number of judicious injections postoperatively, particularly of the sclerosant foam[173] in small amounts, is indicated to remove the occasional few persistent varicosities.

During pregnancy[174] it is considered advisable to postpone stripping until at least three months after delivery. Elastic support, preferably in the form of heavy elastic stockings, may be used in the interim. It is technically difficult to perform an adequate operation during pregnancy, and the danger of postoperative thrombosis and embolism is great.

Venous Thrombosis and Pulmonary Embolism

Owing to the increase in life span during the past half century more patients of older age are admitted to hospitals, especially for neoplastic disease, so that the incidence of thromboembolic disorders has risen.[191] Though the etiology of this condition remains incompletely understood, the rate of blood flow and the state of the venous endothelium appear to be important contributing factors.[135,187,197,199,209,213,217,220,222,225,231] McLachlin and Paterson,[211] in 100 autopsies on men over forty years of age, found 34 with venous thromboses. Of the 76 thrombi found in these 34 patients 6 were in the pelvic veins, 49 were

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in the thigh veins, and 21 were in the leg veins.[233] Venous thrombosis may vary from the silent type, which causes few signs and symptoms, to the classic picture of deep femoroiliac thrombosis — phlegmasia alba dolens. Each of these two types represents a different stage in the same underlying disease. Venous thrombosis may be massive even to the extent of producing gangrene of the extremity.[186,193,227] The diagnostic features[190] of early venous thrombosis of the lower extremities are swelling, tenderness, calf pain on foot dorsiflexion, distended superficial veins and a concomitant rise in the temperature, pulse and respirations. The development of chest pain, especially with hemoptysis, is an almost certain indication of pulmonary embolism.

Prophylaxis should consist primarily of measures to prevent sluggishness of the blood flow in the lower limbs.[210,212,224,226] One can best accomplish this by instructing patients to push on a footboard while in bed to exercise their calf muscles; slight elevation of the head of the bed on low blocks will facilitate this maneuver. Early ambulation[202,203,223] should also be practiced, with emphasis on actual walking. Elastic stockings[228] have also been recommended because by their use the rate of venous blood flow is increased. Simple standing and especially sitting are dangerous since they encourage intravascular stasis. Any pressure on the popliteal space, as from pillows, should be avoided; abdominal binders, which decrease venous return, can also be harmful. The importance of prophylaxis is emphasized by the following figures. In the first place Ochsner, DeBakey and DeCamp,[215] after an analysis of 500 cases of venous thrombosis, stated that in 43.3 per cent of the fatal cases not associated with heart disease there was no clinical evidence of phlebothrombosis. Secondly, Roe and Goldthwait[218] report that 53 per cent of 92 deaths from pulmonary emboli were without clinical warning. Finally, in two large series discussed by Kirby and Fitts,[200] there was no warning of fatal embolism in 71 per cent and 82 per cent of the patients. Therapeutic measures recommended are femoral-vein interruption[175,177,183,189,198,206,207] and anticoagulants,[178,180,182,188,195,216] either singly or in combination.[181] Superficial femoral-vein interruption is carried out at a site that is flush with the entrance of the profunda so that no cavity of "dead space" is produced where a nidus of clot can form. In bed-ridden patients, such as those with heart disease and those who are found at operation to have thrombosis of the profunda vein, the common femoral vein is interrupted just distal to the entrance of the saphenous vein. Ligation of the common femoral vein proximal to the saphenous vein may result in the loss of either the patient's limb or his life. In addition to the classic picture of early lower-extremity venous thrombosis previously mentioned an indication for femoral-vein interruption is the occurrence of pulmonary embolism alone without thrombosis of the deep leg veins. In patients who are first seen forty-eight hours or more after the development of femoroiliac thrombosis anticoagulants are recommended, rather than operation, unless pulmonary embolism has occurred, when the inferior vena cava should be interrupted. It has been found that after this length of time the clot is too adherent to be removed.

Both heparin and Dicumarol are administered initially, unless contraindicated, and the former is discontinued when the prothrombin time has reached a satisfactory level — below 20 per cent of normal. Dicumarol, though the most satisfactory anticoagulant for routine use, is not without disadvantage[179,230] and hazards.[192,194,208,219,234] Cases ending in death have been described by London,[208] Lilly and Lee[204] and Wright and Rothman.[232] In a series of over 3000 patients who underwent major surgery and received Dicumarol postoperatively, Wise et al.[229] stated that 6 (0.18 per cent) had vascular complications; this included 1 fatal infarct. In a control group of over 2000 patients who did not receive the drug there were 34 vascular complications (1.6 per cent), including 5 deaths from pulmonary embolism. Allen,[176] in a series of over 1000 prophylactic femoral-vein interruptions, gave an account of 5 deaths from pulmonary embolism after operation. In another group of 1500 patients Allen reported 7 cases of fatal embolism after therapeutic femoral-vein interruption. In the total of 2578 procedures, however, there were no deaths or amputations from the ligation itself. It can easily be seen that neither an anticoagulant nor ligation is the ideal prophylaxis or treatment for venous thrombosis. Venous interruption, though not appearing quite as effective, is certainly not as dangerous.

Acute thrombophlebitis of the superficial veins of the lower extremity poses a slightly different problem, and various methods of therapy have been recommended.[201,221] This condition is effectively treated by stripping of the main saphenous trunk into which the involved tributaries drain, together with actual excision[196] of the thrombosed veins. The operation is performed during the acute stage. By this method the period of disability is decreased from weeks to days. If the superficial phlebitis develops in a patient whose saphenous trunks have previously been removed and if the involvement is not extensive enough to warrant local excision compression bandages or heavy elastic stockings, from the toes up to a level higher than the inflammatory process, are advised, and active ambulation encouraged. This is a departure from the widely accepted method of former years in which these patients were confined to bed with the involved limb elevated. Immobilization not only incapacitates the patient but also slows the circulation in the limb, permitting the thrombus to propagate.

In patients exhibiting superficial migratory phlebitis of the type sometimes associated with Buerger's disease, long-term Dicumarol therapy[184] is recommended. This method of treatment over a long

period has also been employed by cardiologists when coronary thrombosis is likely to develop.[214] Prothrombin determinations may be made at weekly intervals, and satisfactory levels of prothrombin activity may be maintained indefinitely.

Postphlebitic Syndrome

Ulcerations of the lower extremity have plagued humanity for centuries. Boyd et al.,[239] in a series of 308 cases, classified leg ulcers in three groups: arteriosclerotic, varicose and postphlebitic. The last type is the most common variety. According to Ochsner and his associates,[257] who studied 246 patients, the original phlebitis occurred postoperatively in 30.9 per cent of the patients, post partum in 16.3 per cent, spontaneously[242] in 12.2 per cent, post-traumatically in 9.3 per cent and from varicose veins in 3.7 per cent.

Many forms of therapy advised for this condition have failed because of lack of understanding of the basic pathologic physiology. During the acute thrombophlebitic process there is destruction of the valves of the deep and communicating venous systems.[235,256,259] Canalization of the deep veins produces a constant state of venous hypertension as long as the patient is in the erect position. The venous pressure in the superficial veins of a normal lower extremity drops precipitously when ambulation is begun and remains at a low level until walking has stopped. In the postphlebitic patient the ambulatory venous pressure falls very slightly, if at all.[240,241,246,248,249,258,263,264,265]

Prevention of engorgement of the superficial venous system, which, unlike the deep veins, has no unyielding fascial sheath, is the aim of proper therapy. The state of continuous superficial venous hypertension that has been transmitted through the valveless deep and communicating systems is responsible for the pain, edema, pigmentation, varicosities and ulceration of the postphlebitic extremity.[247,252] Alleviation may be obtained either temporarily in the form of elastic bandages on the lower leg, or more permanently by surgical division, subfascially, of the communicating veins of the lower leg, combined with stripping of the saphenous systems and interruption of the superficial femoral vein.[245] A plan of therapy that has been successfully carried out in a large number of patients has consisted of preliminary healing of leg ulcerations with compression bandages applied on office visits, followed by hospital admission for the operation as outlined.[251] Aftercare includes the wearing of an adequate elastic stocking on the lower leg as long as edema is present. Scott[261,262] has devised a pulsatile air-pressure legging for this purpose. Bauer[236,237] advocates ligation of the popliteal rather than the femoral vein. This procedure was performed on 245 extremities, of which 84 per cent remained healed, with no recurrence of stasis symptoms. DeTakats[243] has obtained good results with this therapy in a small series.

Several methods of phlebography have been introduced for determining the status of the valves in the deep and communicating systems.[238,244,250,254,255,256,260] A grave hazard of this examination is pulmonary embolism, which may be fatal. Interpretation of phlebograms is also extremely difficult. Clinical examination of the patient can be sufficient, and a simple tourniquet test may be employed to ascertain valvular competency. In the supine position the patient raises the involved extremity to empty the veins of blood. A tourniquet is then placed just distal to the knee, and the patient is asked to stand. If the superficial veins below the tourniquet remain collapsed the valves of the deep veins are competent. Immediate filling of these superficial veins on standing indicates that the deep and communicating valves are incompetent.

In the treatment of the postphlebitic syndrome there are few if any indications for lumbar sympathectomy, which should be avoided in patients with this condition. It has been observed that in some persons dermatitis and ulcerations of the leg and foot develop and refuse to respond to any therapeutic measures, so that a new disease has been described, known as the postphlebitic-postsympathectomy syndrome.[253]

Portal Hypertension

Portal hypertension may be secondary to either an intrahepatic obstruction, as in cirrhosis of the liver, or to an extrahepatic block, as in thrombosis of the portal vein (so-called Banti's syndrome).[283,305,311] Liver-function tests help differentiate these two types. The esophageal varices that follow portal hypertension are a serious threat to life, for exsanguinating hemorrhage occurs from them.[279] From 1934 to 1945, 108 patients with cirrhosis of the liver and 20 with Banti's syndrome were admitted to the Massachusetts General Hospital. This group was reviewed by Shull, according to Linton,[301] who found that 45 per cent of the deaths in the cirrhotic patients and 71 per cent of the deaths in those with Banti's syndrome were from bleeding esophageal varices. Wagenknecht et al.[325] regard the acid peptic action of the gastric juice on the esophageal mucosa as an important factor in the initiation of bleeding in esophageal varices but it seems that the rupture may be mechanical since in many patients it occurs in association with the coughing of an upper respiratory infection.

A number of surgical procedures[266,290,293,320] have been attempted in the past, but the establishment of a portacaval or splenorenal anastomosis[272,296,298,314,317] is considered to be the most effective definitive procedure for the treatment of portal hypertension. When the portal vein has been destroyed by thrombophlebitis a splenorenal anastomosis is frequently the only type of shunting procedure that can be done. For this reason splenectomy alone should never be performed in a case of extrahepatic portal-bed block because it produces thrombosis of the splenic vein and consequently spoils at a later date the opportunity of

performing a satisfactory splenorenal anastomosis. In cirrhosis of the liver both the portal vein and the splenic vein are available for a shunting operation. An index to the size of the splenic vein may be obtained preoperatively by abdominal x-ray films outlining the size of the spleen itself. One may safely assume in the majority of cases that if the spleen is large the splenic vein will also be large. Conversely, the appearance of an exceptionally small spleen would discourage consideration of a splenorenal anastomosis in favor of a portacaval shunt. Splenoportography is recommended to determine the state of the splenic and portal veins,[326] but it is not without serious risk owing to hemorrhage from the splenic puncture.

A splenorenal shunt, when feasible, is preferred to a portacaval anastomosis because the portacaval shunt may be done at a later date if needed, the arterial inflow of the portal system is lessened after removal of the spleen, the oversized organ may be producing signs of hypersplenism, and there is evidence that cirrhotic livers do not tolerate the portacaval as well as the splenorenal procedure. Blakemore[275] reports some interesting statistics. After 54 splenorenal anastomoses for intrahepatic block 1 patient died from liver failure, whereas in 16 portacaval anastomoses for intrahepatic block, 8 patients died from liver failure.

In patients with Banti's syndrome, whose spleens have been previously removed, an attempt may be made to anastomose the superior mesenteric vein to the vena cava. If this is not possible transesophageal suture of the esophageal veins is recommended. In 15 cases of bleeding with extrahepatic obstruction after splenectomy Blakemore and Fitzpatrick[274] constructed shunts between the portal and caval systems, utilizing the portal vein in 1 case, the splenic vein in 3 cases and lesser veins in the remainder. One patient died and an occluded anastomosis was found at autopsy. Of the 14 cases of bleeding after splenectomy in living patients 10 are described as failures. Rousselot[317,318] has used autogenous venous grafts joining the portal and caval systems in 7 patients, 5 of whom have had excellent clinical courses.

Blakemore et al.[276] have recently reported their experiences with anastomoses joining the portal and caval systems performed between 1945 and 1952 on 49 patients with extrahepatic block and 152 with intrahepatic obstruction. Of the former group a total of 6 patients died; this included both the immediate and the follow-up mortality. In the latter a total of 61 patients succumbed.

The surgical treatment used in 90 patients with bleeding esophageal varices has been discussed by Linton.[301] The diagnosis in 24 was Banti's syndrome; the remaining 66 had cirrhosis. Splenorenal anastomoses were performed in 68 patients, and direct portacaval anastomoses in 22. In the entire series there were 13 postoperative deaths. However, only 3 of these deaths occurred in the last 60 shunts; in the entire group there were 8 late postshunt deaths, 3 of which were unrelated to the varices or to cirrhosis of the liver.

A different problem is presented by the patient who is admitted to the Emergency Ward with active bleeding from esophageal varices. If a rapid response does not follow immediate transfusion, as shown by elevation of blood pressure and fall in pulse rate, along with a rise in hemoglobin level, balloon tamponade[297,308,321] is instituted, and the operating room is alerted for emergency transthoracic transesophageal ligation of the bleeding source. It is recommended that when insertion of the balloon tube is necessary to control the hemorrhage, emergency ligation should be performed within the ensuing several hours. It should be stressed that the operation must be performed during this period because prolonged tamponade produces edema, friability and even ulceration of the lower esophagus. The procedure under such conditions is technically difficult, and postoperative complications, such as leakage of the esophageal suture line, are likely. This method of therapy with transesophageal ligation of the bleeding varices has been reported by Linton and Warren[300,301] in 15 cases. There has been 1 operative death. Subsequent shunt operations have been carried out in 6 patients and are planned in 2 others. A shunting procedure could not be performed in 3 patients with Banti's syndrome, each of whom had undergone a previous splenectomy. Two late deaths occurred, 1 from liver failure not related to the operative procedure, and the other from massive bleeding two months after the emergency ligation; this patient refused to have a shunt when it was recommended four to six weeks after the emergency suturing.

It is of extreme importance that the patients with cirrhosis undergoing such surgery be carefully selected.[273,299,309] The evaluation of the extent of liver disease is essential because severely depleted hepatic function indicates a grave operative risk. Plasma albumin should be more than 3 gm. per 100 cc., and ascites, if present, should be reversible under medical therapy before surgery is considered. When ascites is recalcitrant to conservative measures a shunting procedure is not recommended. Contrary to some views, it is believed that the ascites may be increased rather than decreased by the portacaval anastomosis. The advent of hypotensive spinal anesthesia[293,302,307,319] has been of remarkable benefit, both to the surgeon and to the patient. The minimal amount of bleeding that takes place shortens considerably the operating time, with consequent lessening of the surgical risk to the patient. Ether is believed to have a harmful effect on the cirrhotic liver and is not advised as an anesthetic agent for long procedures on these patients. Laboratory evidence to support this policy has not as yet been forthcoming.[288,289]

A vast amount of experimental material on the physiology of the liver has been published in recent years. Estimations of liver blood flow have been made

by a variety of methods, and portal hypertension has been produced in laboratory animals.[270,271,277,278,282,285,286,287,291,294,295,306,310,315,324]

The status of hepatic-artery ligation in the treatment of portal hypertension is a controversial subject.[267,268,269,280,281,303,304,312,313,316,322] The results are not encouraging, as reported by several surgeons. Desforges et al.[284] state that hepatic-artery ligation apparently did little to ameliorate the disease in the 4 cases presented. Taylor and Rosenbaum[328] recommend abandonment of the procedure until it can be determined more definitely which patients it might possibly help, and in which ones it is definitely contraindicated.

Lymphedema

Chronic lymphedema remains a challenge to the surgeon because it continues to resist cure by any form of therapy. DeTakats,[328] in a study of lymphedema based on 150 personally observed patients, subdivides the group according to the following classification: congenital (28 cases), inflammatory (58 cases), degenerative (22 cases), traumatic (11 cases) and unknown (31 cases). There were 35 males and 115 females in the series. No patients with postphlebitic syndrome were included. The author calls attention to the beneficial effects of elevation, elastic compression, mercurial diuresis, heparinization and sympathetic blocks, each having its proper place used alone or in combination. In the chronic late cases that cannot be controlled by conservative measures excision of the diseased tissues has been performed. The cosmetic results leave much to be desired, but of 28 patients followed for one to twenty-five years, 17 had satisfactory, 5 doubtful, and 6 poor results.

Boyd[331] has emphasized the fact that in all types of edema there is an early, reversible stage during which the condition can be improved, or at worst held in check. The principles at this stage are mobilization of fluid, prevention of accumulation of fluid on the dependent limb and removal of the causative factor when it is known. The importance of elastic compression during this time cannot be overemphasized. Neglect of these principles leads to the irreversible stage. Aird[331] states that in chronic edema, whatever its cause, one's best hope lies in controlling the edema while it is still of a pitting kind, by elastic bandage (and preferably bed rest) initially and elastic stocking later.

Martorell[329] states that lymphedema differs from venous edema by being less common, harder, scarcely depressible and less reducible by recumbency, and by having a total or rhizomelic distribution. It may be classified as congenital, essential and secondary. Venous edema and lymphedema favor streptococcal infections, which provoke fibrous hyperplasia of the skin subcutaneous tissue and aponeurosis. At length the edema is converted into an irreversible form, totally irreducible by recumbency, which the author calls fibroedema. Campbell and his associates[327] report their technic for the surgical treatment of massive lymphedema of the lower extremities, presenting 3 cases. After a preliminary period of bed rest, elevation and local preparation of the integument the skin, subcutaneous tissue and deep fascia are resected, and skin grafts taken from the body and thigh are sutured into place. Pratt[330] removes the skin of the involved extremity by an electric dermatome and places it directly over the muscle after the intervening tissues have been excised. In 25 such operations he reports that there was no recurrent lymphedema.

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Varicose Veins

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MEDICAL INTELLIGENCE

LAURENCE-MOON-BIEDL SYNDROME

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THE condition now known as the Laurence-Moon-Biedl syndrome was first described by Laurence and Moon in the *British Journal of Ophthalmology* in 1866. Further descriptions were given by Bardet[1] in 1920 and Biedl[2] in 1922. In 1925 Solis-Cohen and Weiss[3] reported 4 cases in one family and referred to the similar cases recognized by Biedl and Raab: "Raab in the course of a very careful study from Biedl's clinic emphasizes the occurrence of 'a syndrome, perhaps familial, hitherto scarcely known of: (a) optic atrophy with pigmentary degeneration similar to retinitis pigmentosa (b) polydactylism (c) obesity (d) genital hypoplasia.'" Mental deficiency was not included, but Biedl later added this to the description and, in fact, laid emphasis on this point "as evidence of a cerebral, rather than a hypophyseal origin of the disorder."

Reilly and Lisser,[4] reviewing the literature, found that up to 1932 only 72 cases had been reported; they added 4 cases of their own. They stated that there were six cardinal symptoms: obesity, genital dystrophy, retinitis pigmentosa, mental deficiency, polydactylism and familial occurrence, but that these were by no means all invariably present. In their series only 25 cases were unquestionably complete, and an additional 10 were questionably so. They stated, that "unless the classical syndrome was present in toto, a 'sine qua non' for the diagnosis of Laurence–Biedl disease necessitated familial occurrence." McCullagh and Ryan[5] noted the uncommon occurrence of the syndrome and referred to an article by Schwartz and Boudreau,[6] who found only 128 cases in the literature up to the middle of 1940.

Anderson[7] noted the frequency of occurrence of combined defects. According to him retinitis pigmentosa was most frequently found as an isolated defect. He referred to the Eugenics Laboratory Memoirs (1922), which described a series of 914 cases of retinitis pigmentosa, 656 with this defect alone. Deaf mutism or mental deficiency occurred in 96 cases (10.41 per cent) and was the commonest associated affliction. In only 9 cases (less than 1 per cent) was polydactylism present. Anderson concluded, therefore, that the occurrence of the signs in a group, as in Laurence–Moon–Biedl syndrome, is obviously rare.

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Little attention has been given to the mental state, beyond the report of the presence or absence of mental defect. However, Menninger,[8] describing the psychologic picture in an eighteen-year-old boy, noted that in addition to the intellectual defect, there was severe emotional instability, that crying could be brought on by the least provocation and this could be changed quickly to laughter by a few words of praise. When with others the patient talked in a loud exhibitionistic manner, monopolized the conversation and staged scenes to attract attention to himself. He had "temper tantrums" or feigned illness if he was called upon to do anything that he did not wish to do. Repeated failures followed his attempts to achieve objectives beyond his capacities. Fury, misbehavior, falsification and childish rebellion invariably ensued. Menninger considered this description "characteristic of the clinical picture so often associated with the typical hypopituitary adiposogenital dystrophy."

CASE REPORT

A 35-year-old woman was admitted to a hospital in 1923 because of episodes of difficult and interfering behavior, severe mood swings when frustrated and many megalomanic ideas. Physical examination revealed a woman who was 175 cm. tall and weighed 98 kg. Her vision was defective, and she wore glasses. The breasts were small and underdeveloped, and the labia minora were absent. Examination of the optic fundi demonstrated pale optic disks and an ill defined retinitis pigmentosa; 10 years later further examination of the fundi showed that the retinitis pigmentosa had increased in extent, gradually approaching the macula. This had progressively reduced her fields of vision to an almost tubular type. A psychometric report in 1933 gave her I. Q. as 74 per cent, with a mental age of 11 years, 11 months, and classified her as "borderline deficiency, classifiable as feeble-minded." Other physical findings were within the normal range, except for a moderate degree of kyphosis of the dorsal spine, arachnoidactyly and high, arched palate; urine and blood counts were normal. The blood cholesterol was 238 mg., the fasting blood sugar 83 mg., and the blood urea nitrogen 14.1 mg. per 100 cc. Blood Hinton and Wassermann tests were negative.

The patient, in general, was pleasant, agreeable and childish. However, when restricted or frustrated, she became irritable, noisy, demanding and obstinate. She retired to her room, turned on the radio very loud and complained that no one was giving her any attention. She talked about owning the hospital and said that no one must leave without telling her and that she must be informed of admissions and discharges. She refused to be called by her correct name (denying that it was correct), but accepted mail addressed to her in her own name. She held many childish ideas, — for example, that Indians were prowling around the grounds at night, — and she wrote to the Governor asking that their property be returned to them. Most of her ideas had been megalomanic, tending not to be fixed; no delusions of persecution were apparent. Her main concern was for the protection of others. Over her 30 years of hospitalization she had given no signs of mental deterioration. Although she had long been regarded as suffering from paranoid schizophrenia, her mental state appeared more compatible with the diagnosis of "pseudologia fantastica." The "delusional" ideas did not appear to have the emotional loading or the intensity of schizophrenia. The absence of persecutory trends, deterioration and hallucinations also tended to favor the diagnosis of a nonschizophrenic illness.

Data regarding the present illness were meager. Apparently, she had always been obese, and it was also noticed from an early age that her vision was defective. Her school record was poor, and she was in need of special tuition, which apparently was not very successful. The menstrual history was said to have been normal. Vision had deteri-

orated slowly over the years, and she was now totally blind. Signs of mental instability became apparent at about 18 years of age, when she first had ideas of being related to the German Kaiser and tended to get into crowds when prominent people were present, stating that she had sent for them to come and that she had a message to deliver to them.

The father had died at the age of 72 of heart disease, from which he had suffered for many years. The mother was alive at 95 years of age, and was said to be in extraordinarily good mental and physical health for that age. There was no blood relation between the parents.

There were 4 children living. The patient was the 2d child; a brother, who was a few years older, was said to suffer from mental defect and obesity; he was totally blind. An ophthalmologist stated that he was suffering from "chorioretinitis, old, quiescent, of both eyes, disseminated, severe, of undetermined cause." No medical report of his general condition could be obtained. The younger brother and sister were apparently normal.

Discussion

This patient had all the characteristic features of Laurence–Moon–Biedl syndrome listed by Reilly and Lisser, except for polydactylism. In addition she showed severe mental instability, which had necessitated continuous hospitalization for the past thirty years. The older brother appeared to be similarly afflicted. He had no severe emotional disturbance, however, and had never needed hospitalization.

Most of the cases previously reported have been in young people, the majority in the series of Reilly and Lisser being under fifteen years of age. Both the patient described above and her brother were over sixty and seemed to be in good physical health except for the defects noted. Little reference has been made in previous articles to the prognosis. Cameron[9] states, however, that the syndrome does not lead to early death, since a case in a patient aged fifty-one has been reported. It has also been thought that most patients become blind by the fifteenth year.[10] In the patients described above, blindness did not appear until late in middle age. The mental state was of a similar pattern to that reported in 1934 by Menninger,[8] except that the megalomanic ideas were more intense and bizarre and the emotional instability greater. The psychologic symptoms might be interpreted as an overcompensation to the severe physical and mental handicaps caused by such a syndrome.

Summary and Conclusions

A case of Laurence–Moon–Biedl syndrome is reported, with a description of the same disorder in a collateral relative.

Unusual features were the age of the patient and the delayed onset of blindness.

The patient showed a psychotic mental picture, with megalomanic ideas and severe emotional instability.

The rarity of the syndrome may be due in part to the failure of recognition of the characteristic group of signs.

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DR. FRANCIS HOME AND PUERPERAL SEPSIS

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BOSTON

THE prevention of puerperal fever is one of the great victories of medicine. It is well recognized that the clear writing of Oliver Wendell Holmes[1] and the courageous exhortations of Semmelweis[2] were the most potent influences in this victory. They were not alone, however, in their belief that puerperal sepsis was a contagious disease and could be prevented by aseptic technics.

Modern historians recognize many other investigators and writers who had already advanced similar views. Castiglioni[3] named Smellie, William Hunter, John Leake, Alexander Gordon (of Aberdeen) and Charles White (of Manchester) as examples of such men. Mettler[4] referred to additional writers — Pouteau, DeLaRoche, Churchill, Hulme, Clarke and Denman. Caldwell[5] recently emphasized the separate writings of Dr. Thomas Watson and Dr. Robert Storrs in 1842.

It is the purpose of this communication to call attention to the work of Dr. Francis Home, of Edinburgh, who had a relatively clear concept of the contagion of puerperal sepsis more than half a century before the classic writings of Holmes and Semmelweis.

Home was born, probably in Edinburgh, on November 17, 1719. After an apprenticeship to an Edinburgh practitioner named Rattray he was appointed surgeon to the regiment of dragoons commanded by John Cope and served with distinction in the War of the Austrian Succession. This tour of military duty was followed by his return to Edinburgh, where he received the degree of Doctor of Medicine in 1750. He continued a distinguished life of teaching, research and practice at Edinburgh that culminated in his being appointed professor of materia medica at the University of Edinburgh in 1768. During this time,

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he was also one of the King's physicians for Scotland. He died in Edinburgh on February 15, 1813.

Dr. Home was responsible for so many ingenious investigations and clear observations that it is difficult to enumerate them all. In his general attitude toward medical teaching and experimentation, he appears to have been far ahead of his time. In the preface to *Medical Facts and Experiments,* he states his principle of selecting cases for study as follows:

> I have selected those cases chiefly which ended unsuccessfully as they afford the fullest picture of the disease, as they often teach more than those which have a contrary issue, as they show the fallacy of trusting to a few observations in the cure of diseases, as they teach us not to be too sanguine in our hopes and promises, as they will at least procure credit which has not always happened to cases that were most successful.[6]

In the preface to *Clinical Experiments, Histories and Dissections,* he offers some sage observations concerning the relation of large hospitals to teaching:

> Nothing at present distinguishes civilized from barbarous nations more than the institution of hospitals for the relief of the sick. They keep proportion with and are the most certain tests of polished and humane manners. Besides the pleasure which arises in a benevolent mind from the contemplation of the relief which hospitals afford, these charitable institutions amply repay the expense which the public bestows on them by promoting the study and practice of medicine. Under one roof are collected a great variety of morbid cases to which students have an easy access and where a wide field is open to physicians for the improvement of the science.
>
> The student has there an opportunity of seeing a variety of diseases without much loss of time and becomes a skillful practitioner before he claims as a physician the confidence of his fellow citizens. He is there taught to avoid many dangerous mistakes into which one who begins the practice without this assistance is apt to befall. . . . Some experiments made in the clinical ward, must meet with more credit than those derived from private practice; as they are performed before so many spectators; as they are reviewed in the clinical lectures; as they are preserved in the private reports—books of each gentleman present, and in those kept in the Royal Infirmary.[7]

His experiences in the War of the Austrian Succession gave him ample opportunity to review military medicine. In regimental orders he issued instructions for the circulation of air around each man and advised the soldiers not to sleep on a bed unless it was 2 feet off the ground. The dragoons were instructed to drink only boiled water. He must have been aware of the part that cold and moisture played in the production of frostbite, of which he described a large series of cases observed in 1743. He made many remarks on gunshot wounds and reported an interesting operation, as follows:

> I was present at a very unusual operation the morning after the Battle of Dettingen; when Mr. Wilson, surgeon to Sir Robert Richard's dragoons, cut off most of the spleen from the dragoon. The wound being very large, the spleen had come out, and being inflamed by the cold of the night, it could not be reduced; there was no possibility to get a fomentation to apply to it. We therefore thought, that cutting it off was the only means to prevent a mortification. The dragoon, though otherwise much wounded, recovered; and I saw him afterwards in good health. He had no stronger inclination for women than before.[8]

Home experimented during his entire lifetime. At an early age, while an apprentice in Edinburgh, he wrote a small treatise on Duns Spa in which he reasoned that the water of Duns Spa must have anthelmintic virtues, because earthworms died more quickly in it than in ordinary spring water.[8] A few of the clinical experiments that he performed were his studies of the following: the relation of the temperature of the body to the pulse rate; the quantity of insensible perspiration in Scotland; the demonstration of the cardiac inhibitory action of squill; and the recognition that the sugar of diabetic urine could be fermented with yeast.

In the field of infectious diseases he made valuable contributions, particularly to the study of measles and diphtheria. He attempted to apply the principle of inoculation to measles and used blood from the area of the rash, conclusively proving that this contained the infectious principle and that the disease was transmissible. The infection so produced ran a milder course than usual, and Home was convinced of the merits of such inoculations.[7] He studied croup for most of his life, noting the remarkable inflammation in the fauces and upper part of the trachea and describing a white, thick, tough membranous crust covering the inside of the trachea for many inches. He even suggested that tracheotomy would have to be performed as an emergency measure to prevent the patient from suffocating.[9] It is of interest that these observations were made half a century before the celebrated work of Bretonneau on diphtheria.

As an example of his powers of observation and deduction his study of melena is of interest. He described 3 cases of "malaene" and realized that the melena was due to blood, and that it came from the intestinal vessels.[7] Although at first glance this might appear to have been an insignificant observation it is to be emphasized that his entire discussion was an argument against the prevailing opinion that the disease was due to *atra bilis* as championed by Hippocrates, Boerhaave, Van Swieten and perhaps Morgagni.

This man of wide vision was interested in other fields besides medicine, as manifested by several of his works: *A Record of Experiments on Bleaching* (1756)[10] and *The Principles of Agriculture and Vegetation* (1757).[11]

Home's thoughts and arguments concerning puerperal fever are very clear. He described 2 cases in his *Clinical Experiments, Histories and Dissections,*[7] together with the autopsy findings on the cases. After discussing other theories of cause and finding much fault with them he came to the conclusion that infection was the most probable. His arguments were along three lines: that the disease was contagious; that it could be eradicated by measures designed to combat contagion; and that it was similar to erysipelas and could be caused by a contact with erysipelas.

Regarding contagion, he held the following opinion:

> This fever has long been observed to prevail, in a greater degree, and to be more dangerous, in hospitals, than in private houses. In 1746, at Paris, none recovered. In the hospitals, at London, during January and February 1770, it was epidemic and fatal to many. It is more fatal in small hospitals than in large. . . . It has been remarked that women delivered among wounded men do not recover.

It was apparently obvious to Home that proper measures could eradicate contagion.

> From the excellent regulations and methods observed by Dr. Young, in the Lying-In ward, very few deaths have appeared since its institution. Yet five died in a short space, at this time. The midwife, and one of the nurses, were seized with fevers suspected to arise from the infection. Reid (one of the cases reported) had been in the house for three weeks, and lay in the room with one who died. . . . Dr. Young thought it prudent to purify the wards, by ventilation, cleaning, white washing. etc. Afterwards this fever totally disappeared and has never since that time occurred there.

He made the following observations on the relation of puerperal sepsis to erysipelas:

> The last opinion, in favor of infection appears to me to be the strongest. Is it of the erysipelatous nature as Pouteau thought? This appears probable, as, This fever has much of the appearance of the erysipelas, from the sensation of the internal heat, from the quickness of its course, etc. . . . Reid [one of the reported cases] had small external tumors [red, painful], which seemed to have some resemblance to the erysipelas. . . . The erysipelas, at that time, was epidemic in the infirmary; and, beyond all doubt infectious. . . . Four of the patients in the beds next to those who had the erysipelas, and the nurses attending them, were infected; and the surgeons of the hospital found, that an erysipelas supervened in every incision.

Although these words are not as meaningful as the subsequent remarks of Holmes, Semmelweis and others, they seem to indicate clearly that Home was aware that puerperal sepsis was contagious, and that methods used in preventing the spread of contagious disease could prevent this infection, which he considered quite similar to erysipelas.

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CASE RECORDS
OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 40361

PRESENTATION OF CASE

First admission. A three-year-old girl was admitted to the hospital for study of oral moniliasis.

Four months previously "belly aches" that were not related to food or accompanied by nausea or vomiting developed, lasting for two to three hours and occurring two or three times a week. The child's appetite had been poor although she had not lost any weight; the stools had been loose. Mouth lesions diagnosed as thrush had first been noted four months before admission and had been treated with gentian violet, without improvement.

Physical examination showed a well developed child, and was negative except for irregular, whitish-gray patches on the oral mucosa, with erosion of the angles of the mouth.

The temperature, pulse, respirations and blood pressure were normal.

The urine had a specific gravity of 1.032 and gave negative tests for albumin, sugar and bile; the sediment was normal. Examination of the blood disclosed a hemoglobin of 12.9 gm. per 100 cc. and a white-cell count of 10,800, with 55 per cent neutrophils, 39 per cent lymphocytes, 4 per cent monocytes and 2 per cent eosinophils. The serum calcium was 9.3 mg., the phosphorus 5.0 mg., and the alkaline phosphatase 7.0 units per 100 cc. Many other blood chemical determinations, urine and stool studies and roentgenograms, including an intravenous pyelogram, were negative. Tuberculin tests were negative in dilutions of 1:1000 and 1:100. A culture from the lesions of the mouth grew out yeasts. The patient was treated with saline mouth washes and vitamin B complex, and since no cause for the moniliasis could be discovered she was discharged on this regimen on the seventh hospital day.

Second admission (two months later). In the in-

terval she had been followed in the outpatient clinic. Her general condition had improved, though the thrush showed little change. The night before admission she complained of pain in the feet and calves, and for a few moments one eye rolled up and was twitching. She was readmitted to the hospital for study.

New physical findings at this time included inversion and spasm of the feet and markedly tender calves. Chvostek's sign and Trousseau's sign were positive.

Urinalysis was essentially as before. The blood hemoglobin was 13.7 gm. per 100 cc., and the white-cell count 16,500, with 86 per cent neutrophils. The serum calcium was 4.8 mg., the phosphorus 13.4 mg., the total protein 6.3 gm., and the alkaline phosphatase 9.1 units per 100 cc. Other blood chemical determinations were normal.

After the child had received calcium gluconate intravenously and calcium lactate by mouth the pedal spasm was relieved. Inulin and phosphorus clearance tests were normal. On the third hospital day the administration of 100,000 units of vitamin D daily was started, but eight days later the dose was increased to 200,000 units a day. A roentgenogram of the wrists showed no bony rarefaction. On the seventeenth hospital day the serum calcium was 7.6 mg., and the phosphorus 7.0 mg. per 100 cc. She was discharged two days later to continue 100,000 units of vitamin D a day, calcium lactate, 3 gm. a day, and Amphojel.

Third admission (one month later). During the interval the moniliasis had grown worse, spreading to the skin and to the vagina. For a while the calcium lactate was withdrawn, but the serum calcium fell to 6.1 mg. per 100 cc., and the therapy was reinstituted. The patient was discharged after the seventeenth day; the serum calcium was 9.4 mg., the phosphorus 4.7 mg., the total protein 5.6 gm., and the alkaline phosphatase 3.9 units per 100 cc. She was discharged on 200,000 units of vitamin D.

Fourth admission (five months later). Shortly after discharge 3 gm. of calcium lactate daily and Amphojel were added to the regimen. Two months after discharge the urinary Sulkowitch test was + + +, and the serum calcium 11.8 mg. per 100 cc. Ten days later the serum calcium was 12.5 gm., and the phosphorus 5.3 mg. per 100 cc. Because of the high serum calcium level the vitamin D and the calcium lactate were withdrawn, and nineteen days later the serum calcium was 10.1 mg. per 100 cc. Forty days after the withdrawal the child complained of pain in the legs, and carpopedal spasm again developed. The serum calcium was now 7.2 mg., and the phosphorus 3.5 mg. per 100 cc. Vitamin D, 250,000 units a day, calcium lactate, 3 gm. a day, and Amphojel were again started. Propylparahydroxybenzoate, 25 mg. three times a day, was added.

Physical examination, urinalysis and routine blood studies were unchanged from the earlier admissions. The child was discharged on the ninth hospital day; the serum calcium was 7.2 mg., and the phosphorus 6.0 mg. per 100 cc.

Final admission (three and a half months later). In the interval she had continued on vitamin D, 200,000 units a day, calcium lactate, 3 gm. a day, Amphojel and para-aminohydroxybenzoate, 25 mg. three times a day. Sulkowitch tests on the urine, done at home, yielded cloudy responses. There was little clinical change until five days before admission, when it was noted that the urinary Sulkowitch test gave a strong response. The dose of vitamin D was halved at that time. Two days later she began to be lethargic and very thirsty, but did not eat. Except for some abdominal distention the physical examination was unchanged. Routine urine and blood studies were normal; the urinary Sulkowitch test was + + + ; the serum calcium was 18 mg. per 100 cc.

The vitamin D and the calcium lactate were discontinued. Treatment with sodium EDTA (disodium dihydrogen ethylene - diamine - tetra - acetate) (Versene)* was begun at once, being given intravenously in a dose of 3 gm. (200 mg. per kilogram of body weight) a day. By the fourth hospital day the serum calcium had fallen to 15.4 mg. per 100 cc. The urinary output of calcium in the twenty-four hours ending on the fifth hospital day was 35 mg. Treatment with sodium EDTA was continued. On the eighth hospital day there was an episode of diarrhea. Two days later the serum calcium was 11.8 mg., the phosphorus 8.3 mg., and the nonprotein nitrogen 72 mg. per 100 cc., and the sodium 117 milliequiv., the potassium 4.5 milliequiv., the chloride 83 milliequiv., and the carbon dioxide 12.3 milliequiv. per liter. The blood pH was 7.40. A plain film of the abdomen demonstrated that the bones were generally demineralized, but the renal shadows appeared normal. The child was becoming oliguric, and the dose of EDTA was reduced to 2 gm. a day. On the eleventh hospital day the oliguria was more severe, and the EDTA was stopped. The output of urine was less than 100 cc., and the extremities were now edematous. Cedilanid, 0.2 mg., was begun on the twelfth hospital day. Two days later the serum calcium was 13.2 mg. and the nonprotein nitrogen 160 mg. per 100 cc.; the sodium was 127 milliequiv., the potassium 4.2 milliequiv., the chloride 90 milliequiv., and the carbon dioxide 11 milliequiv. per liter. The blood pH was 7.22. The patient was now stuporous and anuric and had diarrhea and vomiting. Despite supportive measures blood chemical determinations remained about the same, with a somewhat higher nonprotein nitrogen. She died on the seventeenth hospital day.

Differential Diagnosis

Dr. William H. Baker†: Were the calcium determinations done by the EDTA method or the Fiske–Logan method?

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†Assistant in medicine, Massachusetts General Hospital.

DR. JOHN D. CRAWFORD: The Fiske–Logan method was used most of the time.

DR. ALLAN M. BUTLER: Both methods were used on some specimens.

DR. BAKER: I assume that the urinary sediment was normal.

DR. WINFIELD S. MORGAN: During the last few days of life there were many red cells in the urine.

DR. BAKER: Thank you, I was going to ask about that.

To summarize this long, complicated history and the clinical data, this three-year-old child had a disease over a period of a year that began with an infection in the throat that was diagnosed as moniliasis. Later, neuromuscular irritability and epileptic-like symptoms developed, associated with a hyperphosphatemia and hypocalcemia. I assume that a diagnosis of hypoparathyroidism was made, for she was subsequently treated with calcium both intravenously and orally and with vitamin D. During the period of treatment hypercalcemia developed, the vitamin D and calcium were stopped, and EDTA was started. EDTA was given for eleven days, during which the serum calcium was lowered, but renal failure developed and she died.

For purposes of clarity I shall divide this case into three phases. The first phase was the condition of moniliasis and the development of what I assume was idiopathic hypoparathyroidism. In a review of 52 cases of idiopathic hypoparathyroidism[1] moniliasis associated with this disease was limited to patients in the first decade of life; only 1 patient was in the second decade. There have been 7 cases — and I trust this is the eighth — in which oral or vaginal moniliasis or moniliasis of the fingers preceded the development of the hypoparathyroidism. Sutphin, Albright and McCune[2] have described such cases, and since most of these cases of idiopathic hypoparathyroidism were preceded by monilia infection, they considered it probable that the monilia had a part in the development of the hypoparathyroidism. They mentioned, of course, that the reverse could be true or that the two conditions could be associated with a basic underlying metabolic disorder. They suggested that the preceding oral moniliasis in all the cases was good evidence that this might be an etiologic factor. Another major point is that patients with post-thyroidectomy hypoparathyroidism do not have moniliasis. I am sure that everyone is aware that children have a high incidence of thrush infestation, with or without disease, in their mouths and vaginas. Monilia are usual inhabitants of the mouth, vagina and gastrointestinal tract in 60 to 70 per cent of infants. Hypoparathyroidism does produce ectodermal dysplasia consisting of a rough, dry skin, brittle nails and loss of hair. With some trepidation, since Dr. Albright is a far wiser man than I, I suggest that the moniliasis was a secondary infection associated with the ectodermal changes rather than the cause of the hypoparathyroidism.

The clinical complaint, the neuromuscular irritability associated with positive Chvostek and Trousseau signs, may be explained by the low serum calcium of 4.8 mg. and a high serum phosphorus of 13.4 mg. per 100 cc. Renal tubular acidosis, another condition that may give rise to this syndrome, is unlikely with no other evidence of pre-existing renal disease. There was no evidence of prolonged diarrhea, which also, of course, may cause hypocalcemia and tetany. The patient responded well to intravenous administration of calcium and actually to oral administration of calcium with Amphojel. I am perplexed about the clearance test done at this time. The inulin test showed good glomerular function, and the phosphorus clearance was normal. I have not had any experience with phosphorus clearance, but I assume that in hypoparathyroidism the phosphorus clearance is abnormal — that absence of parathormone with its two and perhaps three actions would induce a phosphorus clearance that was low.

DR. BUTLER: Wouldn't you like to ask if she was receiving vitamin D at this time?

DR. BAKER: Yes.

DR. CRAWFORD: Although the phosphorus clearance was normal, the value was measured under circumstances of metabolic abnormality so that we expected a lower level. We interpreted this test as indicative of some residual parathyroid function but not enough to avoid clinical trouble. In other words, the test indicated that she had hypoparathyroidism rather than aparathyroidism.

DR. BAKER: Excellent!

The second phase of the illness is the period during which the patient received 100,000 units of vitamin D, calcium lactate and Amphojel for hypoparathyroidism and not aparathyroidism. She certainly received a large amount of vitamin D. It seems to be the impression of some who see this disease more than I do that these patients may be more susceptible to overdoses of vitamin D than the normal person. This is a supposition that I really cannot prove. The reactivity to the vitamin D and the production of intoxication with hypercalcemia is dependent on the level of the intake of calcium. I am sure this child was drinking milk — about a quart a day?

DR. CRAWFORD: Yes.

DR. BAKER: I can probably add 1 to 1.5 gm. of calcium intake to the 3 gm. of calcium that she was taking. Vitamin D has a greater toxic effect when the calcium intake is increased. Bauer et al.[3] many years ago assayed irradiated ergosterol in human patients and showed that with an increase in the calcium intake in the diet the susceptibility of the patients to vitamin D intoxication increased.

DR. BUTLER: I wonder why, if this child was getting so much milk, she was given Amphojel without

being put on a reduced milk intake and increased calcium intake by the addition of calcium lactate.

DR. BAKER: That is puzzling.

DR. CRAWFORD: It was our preference to give this child a normal diet so far as possible and offset the absorption of phosphate by adding the Amphojel.

DR. BAKER: That is all Amphojel does; it produces an insoluble aluminum phosphate, which lowers the amount of phosphate that is absorbed. It must be a difficult problem and one I should not like to face—to manage a child with hypoparathyroidism on vitamin D. I am sure that there is immense difficulty in collecting urine specimens and interpreting the Sulkowitch reactions; it is much easier to manage therapy in an adult.

DR. CRAWFORD: The difficulties in following this child were great. They were increased after the parents read in Dr. Alvarez's column about the dangers of excessive vitamin D. Most of the time, although it is not manifest in the protocol, we were faced with hypocalcemia rather than hypercalcemia.

DR. BAKER: The third and major phase of this patient's illness was what I interpret to have been vitamin D intoxication due to a combination of excess vitamin D, an increased calcium intake and Amphojel. May I see the x-ray films of the patient?

DR. JOSEPH HANELIN: I think we might compare the first and last films of the lumbar spine and pelvis that were made approximately fourteen months apart.

DR. BAKER: That is while she was on vitamin D?

DR. HANELIN: The first set was taken when she was first seen; the other set must have been very close to the time of death. There is not much striking skeletal change although one has the distinct impression that the bones were decalcified at the last admission.

DR. BAKER: Was this film taken when she was acidotic?

DR. HANELIN: I think so. It would be hard to make a diagnosis of hypoparathyroidism from the appearance of the skeleton. There may be some prominent trabeculation, which we sometimes see with hypoparathyroidism, but I should not have said so. There was some decalcification later on. The epiphyses that were formed during the course of the illness show no particular changes.

DR. BAKER: No shortening of the metacarpal bones?

DR. HANELIN: No; there is nothing to suggest pseudohypoparathyroidism in the skeleton.

DR. BAKER: I shall interpret the decalcification of the skeletal system as a result of overdosage of vitamin D, with perhaps acidosis playing a minor role.

What interests me most is the treatment of the hypercalcemia that resulted in the patient's death. EDTA is a chelating agent that has a strong avidity for calcium; 1 gm. of sodium EDTA will chelate approximately 100 gm. of calcium. This has been used successfully to reduce serum calcium levels temporarily. In another patient with extensive metastatic carcinoma of the bones to whom we gave a large amount of sodium EDTA intravenously the serum calcium level was indeed lowered when determined by the EDTA and Fiske–Logan methods, but the serum calcium was not lowered when determined by pre-ashing of the serum. This patient had calcium coming out of the bones because of the osteolytic nature of the tumor. As the calcium was chelated with EDTA more calcium entered the serum so that in the end phase by the EDTA and the Fiske–Logan methods the serum calcium was 10.4 mg. and 26 mg. per 100 cc. after ashing. That is why I asked about the simultaneous determinations in the patient under discussion, who obviously had a different disease.

DR. CRAWFORD: Determinations were made on several serum samples by both the EDTA and a flame photometric method; there was never a discrepancy of more than 10 per cent in the values obtained.

DR. BAKER: EDTA was given over what period?

DR. CRAWFORD: Almost continuously during a twenty-four-hour period.

DR. BAKER: This case, then, corresponds to one with which Dr. Albert Schilling and I ran into difficulty, so that I am greatly inclined to a diagnosis of EDTA toxicity in this case. The patient under discussion received an eleven-day course of 3 gm. of EDTA — about the same dosage that we gave to the patient with metastatic carcinoma and hypercalcemia over a thirteen-day period (250 mg. per kilogram of body weight). The latter patient, when she died, had changes in the kidneys that I believe were partly due to EDTA toxicity. The patient under discussion had diarrhea such as I have seen in other patients treated with EDTA, but I am puzzled about its pathogenesis.

The serum calcium in the patient under discussion certainly fell, but uremia developed, with a rising nonprotein nitrogen and decreasing sodium and chloride. The lowered chloride makes me happier about discarding renal tubular acidosis as a diagnosis, since it is almost constantly associated with a hyperchloremic acidosis and not a hypochloremia. On the eleventh hospital day oliguria developed, and there were red cells in the urine. When did the red cells appear?

DR. CRAWFORD: Approximately on the eleventh day. Before the clinical recognition of the oliguria the urine had been fairly normal.

DR. BAKER: The red cells appeared about the eleventh day, with oliguria, azotemia and acidosis associated with widespread edema. One obviously should think of a kidney defect such as tubular damage. Tubular damage produces this entire picture, and I think it was due to EDTA toxicity in the distal tubules with a shutting down of urinary function, resulting in uremic acidosis and death. Disturbing factors are the low sodium and low chloride. I wonder if there was a "sleeper" of Addison's disease. Did the blood pressure change at all?

DR. CRAWFORD: No.

DR. BAKER: What was the eosinophil count?

DR. NATHAN TALBOT: It was at a normal level of 300 per cubic millimeter.

DR. BAKER: I merely mention that because some of the patients with hypoparathyroidism also had associated Addison's disease. Three cases out of 52[1] to my knowledge have been so described, 1 by Talbot, Butler and MacLachlan.[4] I shall not dwell on that since I cannot make a positive diagnosis.

Merely to be complete I shall mention another metabolic process — the Fanconi syndrome, in which large amounts of amino acids, phosphates and sugar pour out into the urine and produce hypophosphatemia; in this case there was hyperphosphatemia.

My interpretation of this case is that the patient had idiopathic hypoparathyroidism associated with moniliasis; vitamin D overdosage and intoxication resulting in osteomalacia; and EDTA toxicity producing renal tubular damage. As I talked about renal tubular damage I left out a pertinent point — that is, that there is a shift in the pH of the urine as it descends from the proximal to the distal tubules. EDTA chelates calcium maximally at a pH of 7.4, and the chelation depends on an alkaline environment: the more alkaline the solution, the more chelation; conversely the more acid the solution, the less chelation. When the EDTA that had chelated the calcium arrived at the distal tubule I am sure that there was some release of calcium if the pH of the urine was about 5 or 5.5. That value was not given to me, and I meant to ask about it.

DR. MORGAN: The urinary pH was 5.5 on the eleventh hospital day.

DR. BAKER: At a pH of 5.5 only 40 per cent of the EDTA would be chelated to calcium, in contradistinction to about 80 per cent at a pH of 7.4. So the tubular damage that results from EDTA toxicity, which I think the patient had, may be the result of release of calcium ions in the distal tubule.

DR. CRAWFORD: Clinically an effort was certainly made to keep the urine alkaline during the time that the patient was receiving EDTA.

DR. JACOB LERMAN: Why was the para-amino-hydroxy-benzoate given?

DR. CRAWFORD: It is one of the series of para-amino-benzoic acid esters that the brewers have used for a long time to keep the vats clear of monilia. Later, the manufacturers of antibiotics began to incorporate it in their capsules in an attempt to keep the gastrointestinal tract of patients receiving these drugs free of monilia.

DR. BUTLER: I might make a few comments. In the first place we have given 1 patient with hypoparathyroidism 100,000 units of vitamin D daily for years without toxicity and only partially corrected the calcium and phosphorus levels. Secondly, there may have been some irregularity in the patient's taking the medication at home, and irregularity in dosage might have been misleading in the titration of the proper dosage. Thirdly, since she would not swallow the ordinary pills of vitamin D, she had to be given the medication from a very concentrated solution. The medication was used up immediately before the development of the toxicity, and she was given a new bottle of the concentrated preparation.

Three questions pertaining to the toxicity therefore arise: Was the child taking the medication that was given through the Out Patient Department irregularly? Was there some change in the concentration of the vitamin D solution that was given during the week in which the toxicity developed? And was there some change in the condition of the patient that increased the effectiveness of the vitamin D therapy?

DR. CRAWFORD: I think I can answer two of the questions. Although the vitamin D administration at home was irregular and this complicated the problem of management, at least we were told when the drug was and when it was not given. The second question is answered by the fact that we assayed the contents of the last bottle of medication given to the patient's parents and the result was within 30 per cent of the concentration listed on the label. The final question I cannot answer. Although steatorrhea was noted on the next-to-last admission, shortly before the child was readmitted for hypercalcemia, the mother had reported that the loose, foul, gray stools were no longer present. We ran into one more difficulty. Because hypoadrenalism might complicate the hypoparathyroidism the patient had been repeatedly studied with salt deprivation and other types of adrenal-function tests until as recently as a month before the final admission. The findings were always normal. During the last admission we did note that some hyponatremia developed, but by assay of the urine she was found to be conserving sodium efficiently. We thought that this was good evidence that hypoadrenalism was not present.

DR. MARC P. MOLDAWER: I should like to comment on Dr. Baker's remarks about possible etiologic relations between moniliasis and hypoparathyroidism. It is difficult for me to accept the viewpoint that the sequence is hypoparathyroidism, deficiency state and susceptibility to monilia. There are now at least 2 cases in which normal serum calcium, phosphorus and alkaline phosphatase values were obtained at a time when monilia was widespread, and only subsequently did clinical and laboratory evidence of hypoparathyroidism appear. Secondly, moniliasis is extremely rare after infancy, except in association with debilitating diseases such as tuberculosis and leukemia. The children with this syndrome have in most cases been entirely well and in a good nutritional state at the time the moniliasis developed. Thirdly, we have 1 patient, now twenty-five years of age, who had moniliasis when first seen for symptoms of hypocalcemia in 1942. Despite excellent control of hypoparathyroidism and

of general nutrition over a twelve-year period, he still has extensive monilia infection.

It therefore appears that these patients have either some underlying abnormality predisposing them to both moniliasis and hypoparathyroidism (and Addison's disease) or a susceptibility to moniliasis alone, and that monilia has a predilection for destroying the parathyroid and adrenal glands or in some way or other interferes with their function.

DR. BAKER: It is not found beyond the first decade. In the literature I found only 1 case of monilia infection at the age of sixteen; all the other patients were below ten years.

DR. MOLDAWER: Animal studies have not shown significant EDTA toxicity, even in doses relatively greater and given over longer periods than those given here. Also, it seems unlikely that EDTA per se is responsible for toxic changes. It may act, however, by depleting trace metals or other essential substances.

In this case I wonder if it would be possible to attribute the entire sequence leading to death to vitamin D intoxication and hypercalcemia alone. There was severe hypercalciuria, with precipitation of calcium in the renal tubules, followed by uremia and death.

DR. BAKER: Certainly, hypercalcemia can produce functional impairment of the kidneys over and above that due to the deposition of the calcium salt in the tubules. We know that hypercalcemia in hyperparathyroidism causes an impairment of function whereby the patient is unable to concentrate the urine and will not respond to antidiuretic hormone. Dent et al.[5] treated a patient with sarcoidosis and hypercalcemia with cortisone and found a marked increase in renal function after the initiation of the cortisone therapy and the drop of the serum calcium. The impairment due to the hypercalcemia must be considered along with the EDTA toxicity. Since azotemia developed in this patient while the calcium was falling, however, I should be more inclined to attribute the renal damage to EDTA.

I did not want to discuss the blood changes because it would take too long. The major toxicity that occurred in the patient with the osteolytic metastases was that the blood did not clot; the prothrombin time was infinity, and the blood did not clot unless thrombin was added, whereupon it clotted immediately. A series of studies showed that EDTA has some antithrombin activity and perhaps an antiprothrombin activity as well; whether it is due to the chelation of metal activators is not known at present.[6]

CLINICAL DIAGNOSES

Hypoparathyroidism.
Hypercalcemia.
Generalized moniliasis.
Anuria.

DR. WILLIAM H. BAKER'S DIAGNOSES

Idiopathic hypoparathyroidism, with moniliasis.
Vitamin D intoxication.
EDTA intoxication, with damage to renal tubules.

ANATOMICAL DIAGNOSES

Hypoparathyroidism, with moniliasis.
(Vitamin D intoxication and hypercalcemia.)
EDTA intoxication: acute nephrosis, reticuloendotheliosis, generalized.

Hemorrhage of lungs and pancreas.

PATHOLOGICAL DISCUSSION

DR. MORGAN: There were a good many interesting findings in this patient, but most were microscopical. Grossly, there was moderate enlargement of the mesenteric, retroperitoneal and bronchial lymph nodes, a small hydropericardium and a few blotchy red areas on the lungs. The liver was of about normal weight but on section was rather yellow and greasy. The adrenal glands were about half the normal weight. The kidneys were not remarkable grossly except that on section the cut surface bulged, suggesting the presence of increased intracapsular pressure.

Microscopically, it was found that at least two diseases had existed in this patient, as Dr. Baker predicted: the first I should like to consider as the underlying disease that brought her to the hospital, — hypoparathyroidism associated with moniliasis, — and the second was characterized by widespread changes apparently due to EDTA therapy. To consider the effects of EDTA first, there was a diffuse histiocytosis throughout many organs of the body. The tissue phagocytes of the spleen, bone marrow and lymph nodes, as well as the Kupffer cells of the liver, were diffusely swollen and filled with granular, eosinophilic staining material. Much of the bone marrow appeared to be replaced by these large cells filled with granular material. Just what this phagocytized substance was we are unable to say at this time; however, animal studies with EDTA are being conducted with the hope of being able to determine its chemical nature.

DR. BUTLER: Is that the effect of EDTA or of vitamin D?

DR. MORGAN: To my knowledge this is not seen in vitamin D intoxication, and in view of the fact that we saw a similar process in the case of metastatic carcinoma to bone treated with EDTA, that was mentioned by Dr. Baker, I should think the histiocytosis was due to EDTA.

The glomeruli of the kidneys appeared to be normal, but the tubules, especially the proximal convoluted tubules, showed severe degenerative changes ranging from simple swelling of the lining epithelial

cells to complete desquamation, and usually it was the latter change that had occurred. This picture is similar to that observed in cases of chemical nephrosis such as that seen after the ingestion of mercuric chloride. The distal tubules often contained granular, eosinophilic staining casts, and many of the tubules contained hematoxylin-staining particulate matter having the features of calcium deposits.

The liver showed diffuse, finely granular fatty change. This could have been due to EDTA; however, it may well have been due to the malnutrition that was present terminally. The pancreatic acini themselves and the islands of Langerhans were not remarkable, but all the ducts were filled with inspissated secretion and hemorrhage, which can be attributed to the EDTA in view of its hematologic effect. The blotchy red areas in the lungs observed grossly proved microscopically to be areas of intra-alveolar hemorrhage, and these may have been the result of the terminal uremia or of the hematologic effect of the EDTA. Although there was no evidence of diffuse pulmonary moniliasis, section of one nodule in the lung did reveal the fungus.

DR. BAKER: Did the prothrombin time change in this patient?

DR. CRAWFORD: The prothrombin time was checked frequently during the period of EDTA administration and fell to a value of 50 per cent of normal on the fifth day of treatment. Later, after discontinuance of the EDTA, the prothrombin time rose again to a slightly higher value.

DR. MORGAN: Regarding the parathyroid glands, nothing was found grossly that could be recognized as parathyroid tissue — Dr. Castleman made the examination. The thyroid and perithyroidal tissues were almost serially sectioned — some 100 slides being cut. In several of these we found a few bits of tissue that Dr. Castleman thought might represent very atrophic parathyroid tissue. These did not have the normal architecture of parathyroid tissue, however, consisting of small, apparently encapsulated aggregates of spindle-like cells. We do not know how much significance to attach to them. The adrenal glands showed a severe, uniform atrophy to the extent that the several zones could not be differentiated. There was also considerable loss of lipoid, and in addition there appeared to be a relatively more recent degeneration of cortical tissue adjacent to the cortical medullary junction.

DR. MOLDAWER: Was monilia cultured from what was thought to be parathyroid tissue or from the adrenal glands?

DR. MORGAN: Cultures were not taken of these tissues, but microscopically there was no evidence of monilia as was seen in the lung.

DR. TALBOT: Was the pituitary gland examined?

DR. MORGAN: The post-mortem examination was limited, and we were unfortunately not permitted to examine the head. The thyroid gland microscopically did not appear hypoplastic, and the islands of Langerhans appeared normal.

Regarding hypoparathyroidism, we usually think of 2 types, — the post-thyroidectomy and the idiopathic, — and, as Dr. Baker pointed out, the idiopathic cases usually come to the attention of the pediatricians, since most of them occur in children. I do not believe that everyone will want to discard the possibility of some etiologic relation between moniliasis and hypoparathyroidism quite as readily as Dr. Baker. Certainly, until this question is definitely answered and in view of the considerable number of cases of moniliasis and hypoparathyroidism in the literature, it seems to me worth while to separate the cases of idiopathic hypoparathyroidism into those associated and those not associated with moniliasis. The ramifications of this subject are very interesting. The patient discussed today bears a great similarity to the child who had Addison's disease, hypoparathyroidism and moniliasis described by Talbot et al.[4] Although the clinical studies of the patient just discussed by Dr. Baker did not bear out a diagnosis of Addison's disease, I do not think there is any doubt that she had relative hypoadrenalism.

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"AIR OF FREEDOM"

THE Special Committee to Investigate Tax-Exempt Foundations is directing some of its heaviest fire at the Rockefeller Foundation and the General Education Board, serene in the knowledge that these distinguished institutions have been deprived of any comparable weapons of defense. For, although their critics have had an opportunity to present a case before the Committee, the accused foundations have only the opportunity "to reply promptly and briefly."

These philanthropic organizations seem to have been charged with an "extraordinary catalogue of offenses, ranging from aiding and defending Communist practices in the schools to violation of the anti-trust laws" and, according to Dean Rusk, their president, other charges have been made that "it is hard to believe that the Committee has taken seriously."

The joint statement that the foundations have been permitted to present in rebuttal consists of a main document of 75 pages and 2 supplements that consider specific items. These are sworn to by Mr. Rusk, who, in reference to a criticism that the Cox Committee did not have the opportunity to swear the Foundation's witnesses, replied that his organizations do not have a double standard for testimony, depending on whether it is sworn or unsworn.

The statement that the Foundation and the Board have been permitted to make in their behalf contains 7 main items. It "affirms the dedication to the public interest of these two foundations as non-political, non-governmental, social institutions that 'reflect the application to philanthropy of the principles of private initiative and free enterprise, under public policies which have long recognized the benefits of such activity to a free society.' "

It stresses the point that the foundations have conformed not only to all applicable laws, but to all "authoritatively expressed" public policies. It reviews many of the 41,809 grants made by the foundations and shows that "any allegation of attempted concealment or distortion is without substance." It discusses the "material, social and economic benefits to the country of the tax exempt privilege," showing also that the foundations are actually substantial taxpayers.

In dealing with so-called "intellectual surveillance" it demonstrates the "consistent policy of these foundations not to exercise thought control over studies supported by foundation funds and not to attempt to censor or modify the findings of scholars and scientists whose work the foundations support financially." It suggests the existence in the life of our people of wide areas "which were not intended to be subject to Congressional regulation and control," and it criticizes as confused and inadequate a number of reports prepared for the Committee by the Committee's own staff.

So far as the tax-exempt status of the foundations is concerned, apart from any absurd and extravagant

charges regarding subversive activities, it seems obvious that these institutions do much more good with their money than any national income derived from their taxation could possibly accomplish. Apparently, the attempt to rob them of their tax-exempt status would, if successful, perpetrate on a magnificent scale the old fallacy of killing the goose that lays the genuinely golden eggs.

A final point is worth the time that any member of an investigating committee might care to spend in pondering on it—that "philanthropy can flourish only in the air of freedom." In an investigation of this nature much more than a great philanthropic foundation is on trial; it is the foundation on which democracy rests that is before the tribunal. For too great an abuse of the democratic system releases its powers of self-destruction.

JAMES STEVENS SIMMONS, M.D.

1890-1954

THE sudden death of Brigadier General James Stevens Simmons brings to a close a distinguished medical career. To appraise this career and the contribution of "Steve" Simmons is to study the man in relation to his two consuming loyalties — the United States Army, of which he was chief of Preventive Medicine, and the Harvard School of Public Health, where he was dean and professor of public health after his retirement from military life.

Joining the Army Medical Corps in 1916 after receiving his M.D. degree from the University of Pennsylvania and after serving his internship and residency at the University of Pennsylvania Hospital, Dr. Simmons centered his activity in the study of bacteriology, first at the William Pepper Laboratory and subsequently at military posts and in the Hawaiian Islands after World War I. Without doubt this preparation and experience in "the Islands" marked the genesis of his lifelong interest in tropical public health that ultimately went far beyond the horizons of simple sanitation and exotic infections to a concern with economic and agricultural problems raised by the very successes of man in controlling his decimating diseases. He could see the biologic forces as well as the social and political forces contributing to war or peace; and he came to know as clearly as he knew the results of seeding test tubes with multiplying bacteria that mankind would ultimately squeeze itself into massive war or starvation unless it began to limit its uncontrolled fecundity.

After he finished an appointment as president of the Army Medical Research Board in Manila, General Simmons returned to Washington in 1930 to head the Department of Bacteriology at the Army Medical School. Here he inherited the traditions and contributions of General Sternberg, the founder, and those of his own predecessors, Colonels Craig and Russell and others; and here he assembled the experience and methods of working with men that he utilized so effectively when administering the Division of Preventive Medicine during World War II. He became particularly adept — and this was a pattern that he maintained during the rest of his career — at selecting competent personnel; he picked "winners" and among the members of his staff there were always to be found both the mature and experienced person and the developing junior officer. Although dictatorial enough in their final form, his military orders were framed only after appropriate staff work, discussions and airing of opinions with his "brain trust," to use the term coined for the presidential advisers of the day.

During the war he presided over more councils and committees than can be listed. In such deliberations he was a polite though commanding personality; he was an adept doodler and had a positive genius for turning the doodle into a cartoon — and then revealing it with the half smile of his suppressed puckishness at just the right time to get explosive relief and a tension-breaking chuckle from those present.

At the close of World War II General Simmons became Dean Simmons at Harvard School of Public Health, although still simply "Steve" to his friends. No matter what subject was up for formal consideration he carried with him the dignity and gravity of military rank. Behind that dignity there was a ready smile, especially at a greeting or a good joke; but there was also the determination of a hard worker and self-discipline of a commander of men.

Neither the habit of military life nor the administrative experience gained in a successful career in the Army Medical Corps was to be changed with a suit of clothes. His decisions followed prior consultation with the group that might be called the civilian counterpart of a military staff— and before any committee meeting was called to treat the matter at hand. At the meeting he moved patiently but as swiftly as possible to implement decisions already reached. Sometimes, if it seemed necessary to shorten parliamentary excursions, he might conclude a debate in apparent gravity but undoubtedly with tongue in cheek by remarking, "There is a motion before us to . . . . If I hear no objection I will consider it passed."

Dean Simmons labored, and truly labored, for the school of which he was administrative officer just as he had for the Army in which he shaped his earlier career. His interests and activities were many. An index of the breadth of General Simmons's concept of public health is implicit in the scope of *Global Epidemiology,* of which he was the moving spirit and senior author. In the last analysis he was a doer rather than a philosopher. His enthusiasm was sincere and contagious; his was the broadest scale, the tallest building, the biggest problem and the largest fish.

No portrait of Steve Simmons can be rounded out without mention of his enthusiasm for hunting, fishing and photographing of birds in color — with flash bulbs, Japanese camera and elaborate trigger device. No portrait is complete that does not show him entertaining — students, faculty, officials, dignitaries, foreign visitors — and with his wife at his side always ready with the right name and the sincere personal inquiry that made the recipient feel that he was among friends. Organizer, administrator, scientist, soldier and friend of many, General Simmons commands a salute.

WEDLOCK AND THE BIRTH RATE

THE United States Department of Health, Education and Welfare has summarized, in a recent release, its statistical estimates on births and marriages for the first four months of 1954. During this period the nation's total births exceeded those for the corresponding period of 1953 by some 30,000. Wedlock, on the other hand, experienced no such buoyant rise. After sinking in 1953 to 9.7 marriages per thousand population, the lowest since 1933, the rate fell in the first third of 1954 by another 7.3 per cent, representing the entrance of 25,000 fewer couples into the holy state than in the first four months of 1953.

The apparent anomaly of a rising birth rate and a falling marriage rate does not, however, represent an increasing failure to benefit by clergy. The low marriage rate seems to be accounted for by the relatively fewer young people reaching marriageable age in recent years because of the low birth rate of the depressed 1930's; the high birth rate is attributed to a continuing rise in the number of third and fourth children per family, somewhat in contradiction to the popular belief that American families are having fewer rather than more children.

The unusually high rate of 25.1 births per thousand population in 1953, which looks as if it would be exceeded this year, accounted for the record-breaking estimate of 3,971,000 births in 1953. The strange belief that huge populations are a desideratum of peace, prosperity and contentment, scarcely borne out in the Orient or in such favored populations as that of Puerto Rico, continues nevertheless to be cherished in the strongholds of hypernationalism.

Two doctors in Mississippi have been arrested, and bound over to keep the peace, in consequence of exchanging leaden pills *through muskets.*

Boston M. & S. J., *Sept. 13, 1854*

NONCLINICAL NOTES

EMERGENCY CLINIC

Owing to the death of the only town physician in Sandwich, New Hampshire, an emergency clinic for patients desiring medical attention will be located in the Sandwich school, open on Saturdays from 2 to 4 p.m. A neighboring physician and two nurses have volunteered their services.

APPOINTMENT OF DR. MOLONEY

Announcement has been made of the appointment of Dr. William C. Moloney, formerly, director of research, Atomic Bomb Casualty Commission, as director of Clinical Laboratories, Boston City Hospital. He will continue in his position as clinical professor of medicine, Tufts College Medical School, and director, First and Third Medical Services (Tufts), Boston City Hospital.

NOTICES

SOUTH END MEDICAL CLUB

The next meeting of the South End Medical Club will be held at the headquarters, Boston Tuberculosis Association, 554 Columbus Avenue, Boston, September 21, at 12 noon. Dr. Richard B. Cattell will speak on the subject "Surgical Treatment of Thyroid Disease." All physicians are invited.

POSTGRADUATE MEDICAL INSTITUTE

The Postgraduate Medical Institute, operating under the sponsorship of the Massachusetts Medical Society with the collaboration of Boston University School of Medicine, Harvard Medical School, Harvard University School of Public Health, Tufts College Medical School, Massachusetts Department of Public Health, Massachusetts Academy of General Practice and other agencies concerned with medical education, has announced its offerings of courses in general medicine for the impending pedagogic season.

Courses, which are open to all physicians, will be held in Berkshire District September 29 through December 8, 1954; in Boston October 6, 1954 through April 20, 1955; in the Connecticut Valley region October 8 through December 10; in Essex South January 5 through March 9; in Fall River September 15 through December 15; in Fitchburg November 3 through April 6; in New Bedford October 6 through December 15, and in Norfolk County Hospital, in Braintree, for Norfolk South and Plymouth districts, October 6 through December 15.

Registration for and information regarding all courses should be addressed to Postgraduate Medical Institute, 22 Fenway, Boston 15, Massachusetts.

NEW ENGLAND HOSPITAL HOUSE OFFICERS' CLUB

The next meeting of the New England Hospital House Officers' Club will be held in the small dining room of the hospital on September 21, from 5 to 7 p.m. Dr. Kenneth Farnsworth will speak on the subject "Endometriosis."

AMERICAN COLLEGE OF PHYSICIANS TELECAST

The first nationwide closed-circuit telecast arranged by the American College of Physicians for postgraduate medical education will present a symposium on the management of hypertension. It will be shown at the meeting of the Mississippi Valley Medical Society in the ballroom, Hotel Sherman, Chicago, September 23, from 5 to 6 p.m. All physicians are invited. The telecast will also be shown in other cities.

POSTGRADUATE SEMINAR IN PSYCHIATRY AND NEUROLOGY

The eighth Connecticut Postgraduate Seminar in Psychiatry and Neurology (1954-1955) will begin its program on September 27. Afternoon and evening sessions will be held on Mondays and Wednesdays from September 27 through December 8. Additional weekly sessions will be held on Mondays from January 3 through May 9.

The program is designed for physicians whose interests are mainly those of psychiatry, neurology and related fields of medicine. Advance registration is required. In some sections enrollment is limited. There is no fee or tuition.

Program and registration form may be obtained from the Assistant Dean of Postgraduate Medical Education, Yale University School of Medicine, 333 Cedar Street, New Haven 11, Connecticut.

SOCIETY MEETINGS AND CONFERENCES

SEPTEMBER, 1954–MAY, 1955. Venereal Disease Research Laboratory Courses. Page 285, issue of August 12.

SEPTEMBER 10-28. Consultation Clinics for Crippled Children in Massachusetts. Page 362, issue of August 26.

SEPTEMBER 12-15. Second International Congress of Cardiology. Washington, D. C. Page 410, issue of September 2.

SEPTEMBER 13-15. American Association of Blood Banks. Page 968, issue of June 3.

SEPTEMBER 16-16. American Heart Association. Annual Scientific Sessions. Washington, D. C.

SEPTEMBER 21. South End Medical Club. Page 451.

SEPTEMBER 21. New England Hospital House Officers Club. Page 451.

SEPTEMBER 22. Fall Clinical Assembly. Massachusetts Academy of General Practice. Hotel Statler, Boston.

SEPTEMBER 22. New England Pediatric Society. Page 968, issue of June 3.

SEPTEMBER 22-24. Mississippi Valley Medical Society. Page 246, issue of August 5.

SEPTEMBER 23. American College of Physicians Telecast. Page 451.

SEPTEMBER 23-25. Industrial Health Conference. Page 364, issue of August 26.

SEPTEMBER 24. American Medical Writers' Association. Page 246, issue of August 5.

SEPTEMBER 27–DECEMBER 8. Postgraduate Seminar in Psychiatry and Neurology. Notice above.

SEPTEMBER, 1954–April, 1955. Postgraduate Medical Institute. Page 451.

SEPTEMBER 30–OCTOBER 2. Canadian Society for the Study of Fertility. Page 285, issue of August 12.

OCTOBER 1 and DECEMBER 3, 1954; FEBRUARY 4 and APRIL 1, 1955. New England Society of Anesthesiologists. Page 1054, issue of June 17.

OCTOBER 7 and 8. Pan-Pacific Surgical Association. Page 1092, issue of June 24.

OCTOBER 8 and 9. Academy of Psychosomatic Medicine. Page 748, issue of April 29.

OCTOBER 11-15. American College of Physicians Course. Page 44, issue of July 1.

OCTOBER 16-22. American Occupational Therapy Association. Page 1092, issue of June 24.

OCTOBER 18-29. New York Academy of Medicine Graduate Fortnight. Page 44, issue of July 1.

OCTOBER 22. National Vitamin Foundation Symposium. Page 410, issue of September 2.

OCTOBER 25-27. New England Postgraduate Assembly. Hotel Statler, Boston.

OCTOBER 25-30. Course in Care of Atomic Casualties. Page 285, issue of August 12.

OCTOBER 27. New England Obstetrical and Gynecological Society. Annual Meeting. Hotel Somerset, Boston.

OCTOBER 27-29. International Symposium on the Hypophyseal Growth Hormone. Page 1092, issue of June 24.

OCTOBER 29. Massachusetts Public Health Association. Fall Meeting. Blake's Restaurant, Springfield, Massachusetts.

OCTOBER 31-NOVEMBER 4. American Institute of Dental Medicine. Page 968, issue of June 3.

NOVEMBER, 1954-MAY, 1955. Sanitary Engineering Center Training Programs. Page 122, issue of July 15.

NOVEMBER 2-5. Fourth Annual Bay State Rehabilitation Conference. Hotel Statler, Boston.

NOVEMBER 3-5. National Society for Crippled Children and Adults. Page 44, issue of July 1.

NOVEMBER 12 and 13. Inter-Society Cytology Council. Page 968, issue of June 3.

NOVEMBER 15-26. Laboratory Diagnosis of Tuberculosis. (Course.) Page 246, issue of August 5.

DECEMBER 5. American Academy of Dental Medicine. Page 1092, issue of June 24.

DECEMBER 8. New England Pediatric Society. Page 968, issue of June 3.

DECEMBER 13-17. Congress of Obstetrics and Gynecology. Page 748, issue of April 29.

JANUARY 3–MAY 9. Postgraduate Seminar in Psychiatry and Neurology. Notice above.

JANUARY 10-15, 1955. Course in Care of Atomic Casualties. Page 285, issue of August 12.

FEBRUARY 7-9. McIntyre Saranac Conference. Page 410, issue of September 2.

MARCH 7-12, 1955. Course in Care of Atomic Casualties. Page 285, issue of August 12.

MAY 4 and 5, 1955. American Psychosomatic Society. Page 286, issue of August 12.

JUNE 21-25, 1955. National Association for the Prevention of Tuberculosis. Page 540, issue of March 25.

CALENDAR FOR THE WEEK BEGINNING THURSDAY, SEPTEMBER 16

THURSDAY, SEPTEMBER 16

*8:00-8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:00-10:00 a.m. Combined Medical-Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
*9:00-10:00 a.m. Arthritis Grand Rounds. Robert Breck Brigham Hospital.
*10:00-11:00 a.m. Medical Staff Conference. Sherman Auditorium, Beth Israel Hospital.
*10:00-11:00 a.m. Surgical Rounds. 5th floor teaching unit, Beth Israel Hospital.
*10:30-11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.-12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.
*11:00 a.m. Thoracic Conference. Current Problems in Cardiac Surgery. Dr. Dwight E. Harken and John M. Olney. Main Amphitheater, Peter Bent Brigham Hospital.
*4:00-5:00 p.m. Pediatric Seminar. Burnham Memorial Hospital (Burnham 4), Massachusetts General Hospital.

FRIDAY, SEPTEMBER 17

*8:00-8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:30-11:30 a.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.
*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.
10:30-11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.
*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.
*4:00-5:00 p.m. Child Psychiatry. Burnham Memorial Hospital (Burnham 4), Massachusetts General Hospital.
*4:00-10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Waltham Street.

SATURDAY, SEPTEMBER 18

*8:00-8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:30-10:00 a.m. Orthopedic Staff Conference, Boston City Hospital.
10:30-11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

MONDAY, SEPTEMBER 20

*8:00-8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00-9:00 a.m. Medical and Surgical Clinic on Diabetic Problems. New England Deaconess Hospital.
*8:30-9:30 a.m. Clinic by entire Surgical Staff and Anesthesia Staff. Cheever Amphitheater, Dowling Building, Boston City Hospital.
10:30-11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*12:15-1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*4:00 p.m. Clinicopathological Conference. Pathology Conference Room, Beth Israel Hospital.

TUESDAY, SEPTEMBER 21

*8:00-8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

(Notices concluded on page xxvii)

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OCTOBER 6, 1954 — APRIL 20, 1955
Wednesdays 3-5 p.m.
(Total 50 Hours)
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OCTOBER 8 — DECEMBER 10, 1954
Fridays 7:30-9.30 p.m.
(Total 20 Hours)
HOLYOKE SOLDIERS' HOME, Holyoke
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JANUARY 5 — MARCH 9, 1955
Wednesdays 2-4 p.m.
(Total 20 Hours)
LYNN and SALEM HOSPITALS
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FALL RIVER
SEPTEMBER 15 — DECEMBER 15, 1954
Wednesdays 11:00 a.m.-1:00 p.m.
(Total 24 Hours)
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Wednesdays 2-5 p.m.
(Total 18 Hours)
BURBANK HOSPITAL, Fitchburg
Fee $27.00

NEW BEDFORD
OCTOBER 6 — DECEMBER 15, 1954
Wednesdays 2-4 p.m.
(Total 20 Hours)
ST. LUKE'S HOSPITAL, New Bedford
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NORFOLK SOUTH AND PLYMOUTH
OCTOBER 6 — DECEMBER 15, 1954
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Svartz, N.: Acta. Med. Scandinav. 141:172, 1951.

1952 In a series of 52 patients with chronic ulcerative colitis 30, or 58%, showed significant improvement after treatment with Azulfidine.

Morrison, L. M.: Gastroenterology 21:133, 1952.

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Morrison, L. M.: Rev. Gastroenterology 20:744 (Oct.) 1953.

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Unger, A. H. and Unger, L. Annals of Allergy. 10:128,1952.

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Jenkins, M. C. Jl. National Med. Assoc. 45:120,1953.

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Naterman, H. L. The Journ. of Allergy. 24:60,1953.

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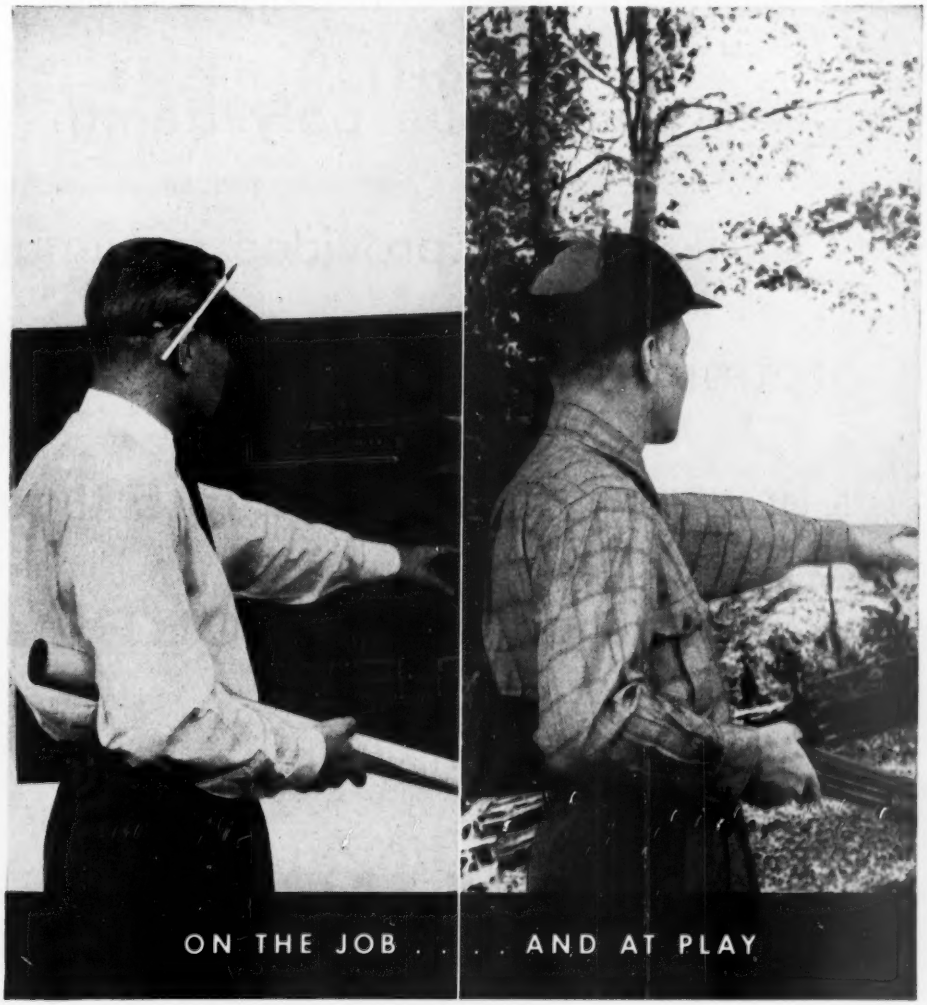

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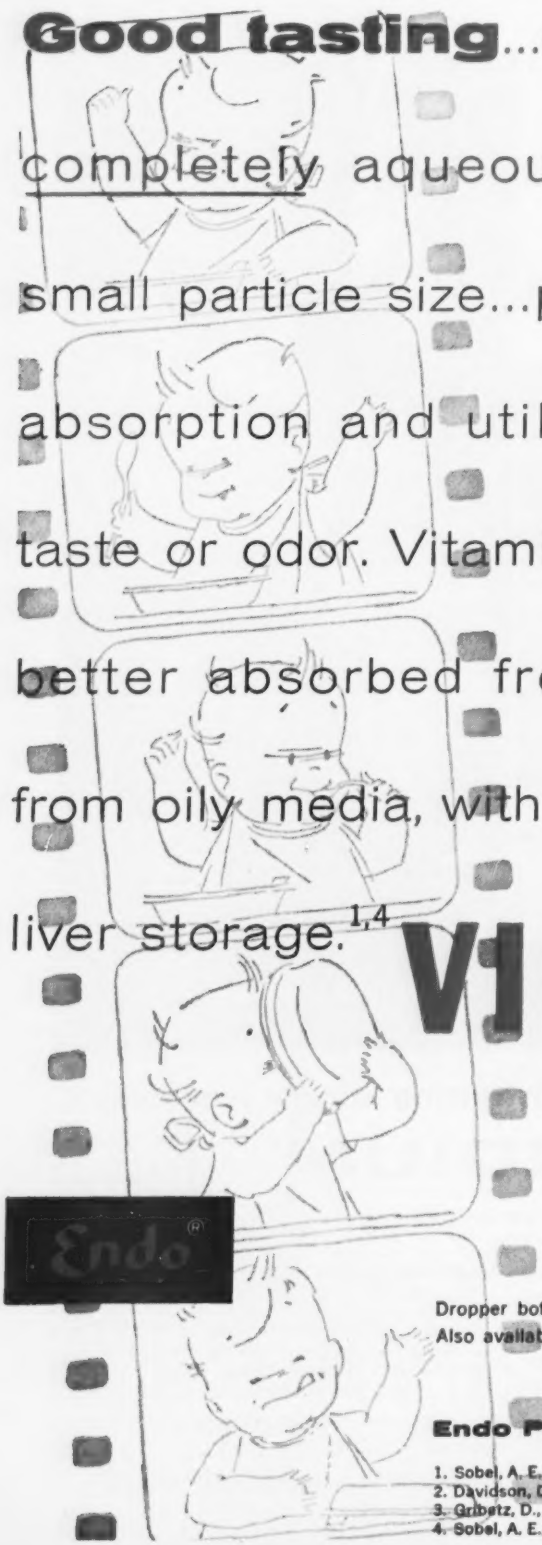

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1. Sobel, A. E., et al.: Am. J. Dis. Child. 80:932, 1950.
2. Davidson, D. M., and Sobel, A. E.: J. Invest. Dermat. 12:221, 1949.
3. Gribetz, D., and Kanof, A.: Pediatrics 7:632, 1951.
4. Sobel, A. E., et al.: J. Nutrition 35:225, 1948.

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*Riese, J. A.: Am. J. Digest. Dis. *21*:81, 1954.

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1. McHardy and Browne: Sou. Med. J. 45:1138, 1952. 2. Lorber and Shay: Fed. Proc. 12:90, 1952.

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NOTICES *(Concluded from page 452)*

*9:00 a.m. Geriatrics Clinic. Peter Bent Brigham Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
12:00 m. South End Medical Club. Surgical Treatment of Thyroid Disease. Dr. Richard B. Cattell. Boston Tuberculosis Association, 554 Columbus Avenue.
*12:00 m. Pediatric Grand Rounds. Cheever Amphitheater, Dowling Building, Boston City Hospital.
*12:00 m.–1:00 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.
*12:15–1:15 p.m. X-Ray Conference. Dr. Merrill Sosman. Main Amphitheater, Peter Bent Brigham Hospital.
12:30–1:30 p.m. Medical Journal Club. Joslin Clinic. New England Deaconess Hospital.
*5:00 p.m. Surgical Journal Review. Mount Auburn Hospital, Cambridge.
*5:00–6:00 p.m. Service Meeting Followed by Clinical Conference (Medical, Surgical, Obstetrical). Faulkner Hospital.
5:00–7:00 p.m. House Officers' Club. New England Hospital. Endometriosis. Dr. Kenneth Farnsworth.

WEDNESDAY, SEPTEMBER 22
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m. Boston State Hospital Psychiatric Seminar. Reception Building Auditorium, 591 Morton Street, Dorchester.
*12:00 m.–1:00 p.m. Clinicopathological Conference. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*12:00 m.–1:00 p.m. Roentgen Diagnostic Conference. 5th floor teaching unit, Beth Israel Hospital.
*12:30 p.m. Weekly Pathological Meeting. Joslin Auditorium, New England Deaconess Hospital.
*12:30–1:30 p.m. Weekly Staff Review of Autopsies. Dr. William A. Meissner. Joslin Auditorium, New England Deaconess Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*1:00 p.m. Massachusetts General Hospital Hand Clinic. Out-Patient Department.
*2:00 p.m. Rectal Clinic. Peter Bent Brigham Hospital.
*2:00–3:00 p.m. Pediatric Conference for Practitioners. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*4:00–5:30 p.m. Fracture Lecture, Boston City Hospital.
*4:00–6:00 p.m. Overholt Thoracic Conference. Joslin Auditorium, New England Deaconess Hospital.
*6:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.

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